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CONFUSION ASSESSMENT METHOD (CAM)

ADAPTAÇÃO E VALIDAÇÃO PORTUGUESA

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À minha avó Deolinda

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RESUMO

Introdução: O delirium surge como uma síndrome neuropsiquiátrica complexa e multifactorial, sendo muito frequente em idosos hospitalizados. Caracteriza-se por alterações da consciência, atenção, cognição e da percepção, que se desenvolvem ao longo de um curto período de tempo (horas a dias) e com curso flutuante. Apesar das graves consequências, como o aumento da morbilidade e mortalidade, não é frequentemente detectado na prática clínica. Deste modo, o recurso a instrumentos de avaliação torna-se fundamental para um maior reconhecimento do delirium. Com este objectivo, surge o *Confusion Assessment Method*/CAM, construído com base nos critérios do DSM-III-R e usado como um método de fácil e rápida administração por qualquer profissional de saúde, mesmo não sendo especialista em Psiquiatria. A partir do CAM, foi recentemente desenvolvido o *Family Confusion Assessment Method*/FAM-CAM, como instrumento de auxílio na detecção do delirium, através das informações facultadas pelos familiares/cuidadores. Neste contexto, o presente trabalho teve como principais objectivos os estudos de adaptação e validação do CAM e do FAM-CAM para a população portuguesa.

Métodos: O processo de tradução destes instrumentos foi realizado de acordo com as linhas de orientação do grupo ISPOR, com treino formal prévio dos investigadores. A versão Portuguesa experimental do CAM foi testada inicialmente num estudo-piloto, para avaliação da validade ecológica, facial e de conteúdo. O estudo principal incluiu uma amostra de doentes idosos (≥65 anos), internados há pelo menos 48 horas, em duas Unidades de Cuidados Intermédios, dos Serviços de Medicina Intensiva e de Cirurgia, do CHSJ no Porto. Foram considerados como critérios de exclusão: pontuação ≤11 na Escala de Coma de Glasgow, cegueira/surdez, incapacidade em comunicar e não ter o Português como língua materna. Todos os doentes foram avaliados de forma cega e independente por uma psiquiatra (com base nos critérios do DSM-IV-TR, como referência-padrão) e, por uma psicóloga (com o CAM), para avaliação da validade concorrente. Foi igualmente testada a validade convergente, comparando o CAM com outras escalas cognitivas, bem como a fiabilidade inter-observador. No estudo do FAM-CAM foram incluídos familiares e/ou cuidadores de doentes hospitalizados apenas na primeira unidade referida, com conhecimento prévio do seu estado cognitivo/funcional e contacto diário durante este internamento. Foram critérios de exclusão: idade <18 anos e não ter o Português como língua materna. Para a validade concorrente, comparou-se o FAM-CAM com o DSM-IV-TR e CAM. Foi ainda avaliado o nível de stresse nos familiares de doentes que desenvolveram delirium, através de uma escala de tipo Likert de 4-

pontos. A Comissão de Ética do referido hospital aprovou esta investigação, tendo sido obtido consentimento informado de todos os doentes e/ou familiares.

Resultados: A versão Portuguesa do CAM apresentou uma boa validade ecológica, facial e de conteúdo no estudo-piloto. No estudo principal (n=208), revelou ainda ter uma sensibilidade de 79%, e uma especificidade de 99%. O valor preditivo positivo foi de 95% e o negativo de 93%. As correlações significativas mais robustas do CAM foram obtidas com o MMSE (r_S=-0.676; p≤0.01) e PMD Ordem Directa (r_S=-0.605; p≤0.01). Revelou igualmente uma elevada fiabilidade inter-observador, com valores de k=1.00 para o total e para cinco itens (restantes com k entre 0.65 e 0.83). A versão Portuguesa do FAM-CAM mostrou um bom nível de compreensibilidade e equivalência conceptual com a versão original. No estudo de validação (n=40), este instrumento revelou uma sensibilidade de 75% e 86% e uma especificidade de 91%, quando comparado, respectivamente, com o DSM-IV-TR e CAM. Um número elevado de familiares (57%) classificou o delirium como uma experiência extremamente stressante.

Discussão: O CAM revelou uma sensibilidade moderada e uma especificidade excelente, em relação aos dados obtidos em estudos prévios de validação. Comparativamente, alguns destes trabalhos excluíam doentes com doenças psiquiátricas (ex. demência), que são facilmente confundidas com delirium. As discordâncias entre avaliações (DSM-IV-TR/CAM) resultaram sobretudo da existência prévia de demência e do curso flutuante do delirium. O CAM teve uma boa validade convergente e, globalmente, uma excelente fiabilidade inter-observador. O valor de k mais baixo foi obtido para o item “pensamento desorganizado”, que poderá ser explicado, em parte, pela necessidade de inclusão de tarefas mais específicas para avaliação desta característica. O FAM-CAM apresentou uma sensibilidade moderada e uma excelente especificidade, tendo sido pela primeira vez validado face a uma referência-padrão. Tal como verificado em estudos anteriores, registou-se uma sobreindentificação de sintomas pelos familiares (com maior número de falsos-positivos) explicada em parte pela ansiedade relacionada com a hospitalização e, ainda, elevados níveis de stresse nos familiares de doentes que desenvolveram delirium.

Conclusão: As versões Portuguesas do CAM e FAM-CAM revelaram boas propriedades psicométricas, podendo ser utilizadas como instrumentos de detecção de delirium em doentes idosos hospitalizados nestas unidades, por profissionais de saúde, com treino prévio. No entanto, torna-se necessário levar a cabo mais estudos, nomeadamente em outros contextos clínicos, para considerar o grau de generalização dos presentes resultados.

ABSTRACT

Background: Delirium appears as a multifactorial and complex neuropsychiatric syndrome, very common in elderly hospitalized patients. It is characterized by alterations in consciousness, with reduced ability to focus, sustain or shift attention, in cognition and in perception, which develops over a short period of time (hours to days) with a fluctuating course. Despite the serious consequences, such as increased of morbidity and mortality, it is often undetected in clinical practice. Thus, the use of assessment instruments becomes essential for better recognition of delirium. In this way, the Confusion Assessment Method/CAM, based on DSM-III-R, appears as an easy and brief method for application by a health care professional, even if they are not a specialist in psychiatry. Recently the Family Confusion Assessment Method/FAM-CAM has been developed, derived from the CAM, as an auxiliary instrument for delirium detection using information from the family/caregiver. In this context, the present work had as main objectives the studies of the adaptation and validation of the CAM and FAM-CAM for the Portuguese population.

Methods: The translation process of these instruments was carried out, according to ISPOR guidelines, with formal previously trained researchers. The Portuguese experimental version of CAM was initially tested in a pilot study, to evaluate the ecological, face and content validity. The main study included a sample of elderly patients (≥65 years), admitted for at least 48 hours into two intermediate care units of Intensive Medicine and Surgical Services of CHSJ in Porto. Exclusion criteria considered were: score ≤11 on the Glasgow Coma Scale, blindness/deafness, inability to communicate and to speak Portuguese. All patients were blinded and independently assessed by a psychiatrist (based on DSM-IV-TR as a reference standard) and by a psychologist (with CAM), to assess the concurrent validity. Convergent validity was also tested, comparing CAM with other cognitive measures, as well as the inter-rater reliability. The FAM-CAM study, included families and/or caregivers of elderly patients hospitalized only in the first mentioned unit, with previous knowledge about their mental/functional state and daily contact during hospitalization. Exclusion criteria were: aged less than 18 years, and unable to speak Portuguese. For concurrent validity, the FAM-CAM was compared with the DSM-IV-TR and CAM. The level of distress in the families of patients who developed delirium was also assessed, using a Likert scale with 4-points. The Hospital Ethics Committee approved this research and informed consent was obtained from the patient and/or from their families.

Results: The Portuguese version of CAM presented good ecological, face and content validity. The main study (n=208) also revealed a sensibility of 79%, and a specificity of

99%. The positive predictive value was 95% and the negative 93%. Significant correlations were obtained, namely with the MMSE (r_S= -0.676; p≤0.01) and DST forward (r_S= -0.605; p≤0.01). A high inter-rater reliability, with values of k=1.00 for the total and for five items (the remaining with k between 0.65 and 0.83) was also shown. The Portuguese version of FAM-CAM revealed a good level of comprehensibility, and conceptual equivalence to the original English version. In the validation study (n=40), this instrument had a sensibility of 75% and 86%, and a specificity of 91%, when compared with DSM-IV-TR and CAM, respectively. A large proportion of the family members (57%) classified delirium as an extremely distressing experience.

Discussion: The CAM showed moderate sensitivity and excellent specificity, when compared with other previous validation studies. However, some of these did not consider the inclusion of patients with psychiatric disorders (e.g. dementia), which are easily confused with delirium. The discrepancies between assessments (DSM-IV-TR/CAM) resulted namely from the pre-existing dementia and fluctuating course of delirium. The CAM had good convergent validity and, globally excellent inter-rater reliability. The lowest value of k was obtained for the disorganized thinking item, which can be explained in part by the need to include specific tasks to assess this characteristic. The FAM-CAM presented moderate sensitivity and excellent specificity, being validated against a reference standard for the first time. As verified in previous studies, an over-interpretation of delirium symptoms by family were found (with a higher number of false positives), explained in part by the anxiety related to the relative's hospitalization, and also high distress levels in families of patients who had developed delirium.

Conclusion: The Portuguese versions of CAM and FAM-CAM revealed good psychometric properties and can be used as instruments for detection of delirium in elderly patients hospitalized in these units, by health professionals with previous training. However, further studies are needed in other clinical contexts to assure generalizability of these results.

RESUMÉ

Introduction: Le delirium est un syndrome neuropsychiatrique complexe et multifactoriel, particulièrement fréquent chez les personnes âgées hospitalisées. Il se caractérise par des altérations de la conscience, attention, cognition et perception, qui se développent sur une courte période de temps (sur quelques heures ou quelques jours) avec une variation fluctuante. Malgré de graves conséquences comme l'augmentation de la morbidité et de la mortalité, il est peu souvent détecté en pratique clinique. De ce fait, l'utilisation d'instruments d'évaluation est fondamentale pour permettre la reconnaissance du delirium. Le *Confusion Assessment Method*/CAM, construit sur la base des critères du DSM-III-R, est ainsi utilisé comme une méthode d'application facile et rapide par professionnel de santé, même si celui-ci n'est pas spécialiste en Psychiatrie. À partir du CAM, on a récemment développé le *Family Confusion Assessment Method*/FAM-CAM, pour aider au dépistage du delirium, à travers les informations transmises par les membres de la famille/soignants. Dans ce contexte, l'objectif principal était d'évaluer l'adaptation et la validation du CAM et du FAM-CAM par la population portugaise. **Méthodes:** Le procédé d'interprétation de ces instruments a été réalisé selon les orientations du groupe ISPOR, avec au préalable une préparation formelle des chercheurs. La version portugaise expérimentale du CAM a été testée auparavant dans un étude pilote, pour l'évaluation de la validité écologique, faciale et du contenu. L'étude principale inclut un échantillon de patients âgés (≥65 ans), internés depuis au moins 48 heures, dans deux Unités de Soins Intermédiaires, des Services de Médecine Intensive et de Chirurgie, du CHSJ à Porto. Il a été considéré comme critères d'exclusion: ponctuation ≤11 sur L'Échelle de Coma de Glasgow, cécité/surdité, incapacité à communiquer et ne pas avoir le portugais comme langue maternelle. Tous les patients ont été évalués sans jugement et de façon indépendante par un psychiatre (sur la base des critères du DSM-IV-TR, comme modèle de référence) et par un psychologue (avec le CAM), pour l'évaluation de la validité concurrente. On a également testé la validité convergente, comparant le CAM à d'autres échelles cognitives, ainsi que la fiabilité inter observateur. Dans l'étude du FAM-CAM, on a inclus des membres de la famille et/ou des soignants de malades hospitalisés uniquement dans la première unité citée, avec une connaissance au préalable de leur état cognitif/fonctionnel et un contact quotidien durant cet internement. Les critères d'exclusion considéraient: âge <18 ans et ne pas avoir le portugais comme langue maternelle. Pour la validité concurrente, on a comparé le FAM-CAM avec le DSM-IV-TR et CAM. On a également évalué le niveau de stress parmi les membres de la famille de malades qui ont développé un delirium, à travers une échelle de type Likert de

4-points. La Commission d'Étique de cet hôpital a approuvé cette recherche, avec le consentement informé de tous les malades e/ou membres de la famille.

Résultats: La version portugaise du CAM a présenté une bonne validité écologique, faciale et de contenu. Dans l'étude principale (n=208), elle a révélé avoir une sensibilité de 79%, et une spécificité de 99%. La valeur prédictive positive a été de 95% et la valeur négative de 93%. Elle a obtenu également des corrélations significatives surtout avec le MMSE (r_S=-0.676; p≤0.01) et le PMD Ordre Direct (r_S=-0.605; p≤0.01). Elle a également révélé une fiabilité élevée inter observateur, avec des valeurs de k=1.00 au total et pour cinq items (le reste avec k entre 0.65 e 0.83). La version portugaise du FAM-CAM a démontré un bon niveau de compréhensibilité et d'équivalence conceptuelle avec la version originale. Dans l'étude de validation (n=40), cet instrument a révélé une sensibilité de 75% et 86% et une spécificité de 91%, comparé respectivement au DSM-IV-TR et au CAM. Une grande partie des membres de la famille (57%) a classifié le delirium comme une expérience extrêmement stressante.

Discussion: Le CAM a révélé une sensibilité modérée et une spécificité excellente par rapport aux données obtenues dans des études précédentes de validation. Cependant, certains de ces travaux ont exclu des patients avec de maladies psychiatriques (ex. démence), qui sont facilement confondues avec le delirium. Les discordances entre évaluations (DSM-IV-TR/CAM) ont résulté surtout de la préexistence de démence et de l'évolution fluctuante du delirium. Le CAM a obtenu une bonne validité convergente et globalement une excellente fiabilité inter observateur. La valeur la plus basse de k a été obtenue par l'item «pensée désorganisée», qui pourra être expliquée, partiellement, par la nécessité d'inclusion de tâches plus spécifiques pour l'évaluation de cette caractéristique. Le FAM-CAM a présenté une sensibilité modérée et une excellente spécificité, ayant été pour la première fois validé par rapport à un modèle de référence. Tel qu'il a été vérifié dans des études précédentes, on a enregistré une suridentification de symptômes par les membres de la famille (avec un plus grand nombre de faux positifs) expliquée partiellement par l'anxiété liée à l'hospitalisation, ainsi que des hauts niveaux de stress parmi les membres de la famille des malades qui ont développé le delirium.

Conclusion: Les versions portugaises du CAM et FAM-CAM ont révélé de bonnes propriétés psychométriques, pouvant être utilisées comme des instruments de détection du delirium chez les malades âgés hospitalisés dans ces unités, par des professionnels de santé avec un entrainement au préalable. Il faut réaliser plus études notamment dans d'autres contextes cliniques, pour nous permettre de généraliser les résultats ci-présents.

INDÍCE

1. INTRODUÇÃO

Com o envelhecimento da população assiste-se inevitavelmente a um acréscimo de doenças crónicas, bem como das complicações médicas associadas a estas, tendo como consequência, o aumento do número de hospitalizações de pessoas mais velhas. Neste contexto, estima-se que 40% dos indivíduos hospitalizados sejam idosos (AHRQ, 2008).

Neste quadro, é inevitável que o delirium (ou estado confusional agudo), uma das complicações mais comuns em idosos hospitalizados (afectando 1/5 destes doentes), tenderá também a aumentar (Ryan et al., 2013).

Além disso, uma elevada prevalência do delirium tem sido sobretudo verificada em doentes com défice cognitivo ou demência prévia (Inouye et al., 2013), patologia que afecta actualmente 35.6 milhões de pessoas em todo o mundo, estimando-se que vá duplicar até 2030 (WHO/ADI, 2012).

De acordo com os critérios do Manual de Diagnóstico e Estatística das Perturbações Mentais/DSM-IV-TR (APA, 2002), o delirium caracteriza-se por uma perturbação da consciência (diminuição da clareza de percepção do ambiente) com redução da capacidade para focar, manter ou transferir a atenção, bem como alteração da cognição (como défice de memória, desorientação, perturbação da linguagem) ou da percepção (que não atribuída a demência preexistente, estabelecida ou em evolução). Esta perturbação desenvolve-se num curto período de tempo (geralmente horas a dias) e tende a flutuar durante o dia. Acresce ainda, pela história clínica e exames físicos/laboratoriais, o facto de ser causada pelas consequências fisiológicas directas de uma doença médica, intoxicação/abstinência de substância ou por múltiplas etiologias.

O delirium assume particular importância pelas graves consequências a curto e a longo prazo, a que têm sido associados os aumentos de duração do internamento hospitalar, das taxas de mortalidade durante a hospitalização (22-76%) e pós-alta (35-40% no primeiro ano), bem como maior precocidade de institucionalização, agravamento do estado cognitivo e funcional destes doentes (McCusker et al., 2012; Leentjens et al, 2012). Neste sentido, o delirium representa um aumento da utilização dos cuidados de saúde e de encargos económicos, com custos anuais estimados em 164 biliões de dólares nos Estados Unidos e em 182 biliões em 18 países Europeus, incluindo Portugal (OECD, 2012; Inouye et al., 2013).

Estas graves repercussões têm contribuído para que de uma forma crescente, o delirium seja considerado como um problema importante no que concerne à

segurança do doente, bem como um indicador de qualidade de cuidados de saúde nestes doentes (Inouye et al., 2013).

Contudo, esta síndrome é frequentemente subdiagnosticada, com cerca de 50% dos casos sem serem detectados pelos profissionais de saúde (Kean et al., 2008). O diagnóstico tardio ou a falta deste, tem sido relacionado com sérias repercussões prognósticas, nomeadamente com o aumento da mortalidade (Kakuma et al., 2003). Inversamente, o seu reconhecimento precoce contribui para a redução da mortalidade e do número de dias de internamento (Rockwood et al., 1994).

A dificuldade de detecção tem sido atribuída a diversos factores, nomeadamente ao curso flutuante do delirium, à sua sobreposição com perturbações neuropsiquiátricas como a demência e a depressão, bem como à falha ou ausência de uma avaliação sistemática na prática clínica, que inclua o recurso a instrumentos de avaliação estandardizados para identificação desta síndrome (Cole, 2004; Ely et al., 2004; Inouye, 2006).

Torna-se assim evidente que a utilização destas ferramentas, surge como um importante contributo não só para a detecção do delirium, mas também para a avaliação da evolução clínica do doente e da eficácia de intervenções terapêuticas aplicadas (Grover et al., 2012), levando deste modo, à redução das suas consequências negativas.

Dos diversos instrumentos existentes, destaca-se o *Confusion Assessment Method*/CAM (Inouye et al., 1990) que foi desenvolvido, com base nos critérios do DSM-III-R (APA, 1987), para ser um método de rastreio de delirium de fácil e de rápida aplicação por qualquer profissional de saúde (mesmo quando não especialista em Psiquiatria), em contextos clínicos e de investigação. O CAM tem sido amplamente utilizado em todo o mundo, em consequência dos resultados positivos provenientes dos numerosos estudos de validação e da facilidade na sua administração e cotação. Além disso, foi já utilizado em mais de 4000 artigos originais, e está traduzido para 12 idiomas em todo o mundo (Inouye et al., 2013), sendo recomendado pelas mais recentes *guidelines* (NICE, 2010).

A partir do instrumento original CAM (Inouye et al., 1990) foi recentemente desenvolvido o *Family Confusion Assessment Method*/FAM-CAM (Inouye et al., 2011; Steis et al., 2012), como um método para auxiliar na detecção de delirium, a ser preenchido com base nas informações/observações dos familiares e/ou cuidadores. O FAM-CAM pode ser administrado pessoalmente, por telefone, ou por via electrónica, o que permite a extensão da avaliação destes casos a contextos onde o delirium dificilmente possa ser avaliado por profissionais de saúde.

Apesar da integração da família no reconhecimento e na prestação de cuidados ao doente com delirium ter sobretudo consequências benéficas, há contudo, que ter em consideração que o delirium tem sido descrito como uma experiência traumática, não só para os doentes, mas também para os seus familiares, que revelam níveis elevados de stresse perante estas situações (O´Malley et al., 2008; Partridge et al., 2012).

Neste contexto, o presente trabalho teve como principais objectivos levar a cabo os estudos de adaptação e validação do *Confusion Assessment Method*/CAM e do *Family Confusion Assessment Method*/FAM-CAM para a população portuguesa.
Para o efeito, este trabalho encontra-se estruturado em duas partes principais. A primeira inclui o enquadramento teórico, composto pelos seguintes artigos já publicados:

1. **Delirium in Elderly People: A Review. Martins S, Fernandes L. Frontiers Neurology, 2012; June 3, Article 101:1-12.**
   Revisão teórica sobre o delirium no idoso, nomeadamente quanto à epidemiologia, características clínicas, diagnóstico, patofisiologia, factores de risco, prognóstico, estratégias de prevenção, intervenção farmacológica e não-farmacológica.

2. **Elderly Delirium Assessment Tools Review. Martins S, Simões MR, Fernandes L. Current Psychiatry Reviews, 2012; 8(2):168-174.**
   Revisão da literatura sobre instrumentos de avaliação do delirium, com análise comparativa quanto ao objectivo (diagnóstico, gravidade ou ambos), população-alvo, dimensões, modo de administração e cotação, tempo de aplicação e características psicométricas.

3. **O Impacto do Delirium na Família/Cuidadores. Martins S, Simões MR, Fernandes L. Revista Portuguesa de Enfermagem de Saúde Mental, 2013; Dez(10):43-48.**
   Revisão da literatura relativa aos estudos existentes sobre o nível de stresse provocado pelo delirium nos familiares e/ou cuidadores de doentes idosos. Os artigos incluídos nesta revisão foram analisados e sintetizados, em particular quando ao tipo de estudo, amostra, modo de avaliação do nível de stresse e principais resultados obtidos.

A segunda parte deste trabalho compreende os estudos de adaptação e validação dos instrumentos CAM e FAM-CAM, incluindo os seguintes artigos:

1. **Pilot-study of European Portuguese Version of the Confusion Assessment Method. Martins S, Moldes P, Pinto-de-Sousa J, Conceição F, Paiva JA, Simões MR, Fernandes L. Acta Neuropsychiatrica, 2014; 26(5): 1-4.**

   Este artigo inclui a descrição detalhada do processo de tradução da versão Portuguesa do CAM, e a apresentação dos resultados do estudo-piloto, realizado numa amostra de 50 idosos hospitalizados, com análise da validade facial, conteúdo e concorrente (sensibilidade/especificidade) desta versão.

2. **Validation Study of the European Portuguese Version of the Confusion Assessment Method (CAM). Martins S, Lourenço C, Pinto-de-Sousa J, Conceição F, Paiva JA, Simões MR, Fernandes L. International Psychogeriatrics (em processo de revisão).**

   Neste artigo é apresentado o estudo principal de validação da versão Portuguesa do CAM, realizado numa amostra de 208 idosos hospitalizados, com apresentação dos resultados relativos à validade concorrente (sensibilidade, especificidade, valor preditivo, razão de verosimilhança), validade convergente e fiabilidade inter-observador.

3. **Family in the Delirium Recognition: European Portuguese Validation Study of the Family Confusion Assessment Method (FAM-CAM). Martins S, Conceição F, Paiva JA, Simões MR, Fernandes L. Journal of the American Geriatrics Society, 2014: 1-5. First published online: 15 Jul 2014.**

   Este artigo inclui o estudo de validação para a população Portuguesa do FAM-CAM, levado a cabo numa amostra de 40 familiares e/ou cuidadores de doentes idosos hospitalizados. São apresentados resultados relativos à validade facial, conteúdo e concorrente (sensibilidade, especificidade, valor preditivo). Este trabalho teve ainda como objectivo secundário a análise do nível de stresse nos familiares de doentes que desenvolveram delirium.

Por último, será apresentado uma conclusão geral, considerando os trabalhos realizados, as implicações para a prática clínica e a investigação em Portugal, com referência à necessidade de estudos futuros para aprofundamento do estudo do delirium em pessoas idosas.

2. ENQUADRAMENTO TEÓRICO

2.1. Delirium in Elderly People: A Review. Martins S, Fernandes L. Frontiers Neurology, 2012; June 3, Article 101:1-12.

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Delirium in elderly people: a review

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The present review aims to highlight this intricate syndrome, regarding diagnosis, pathophysiology, etiology, prevention, and management in elderly people. The diagnosis of delirium is based on clinical observations, cognitive assessment, physical, and neurological examination. Clinically, delirium occurs in hyperactive, hypoactive, or mixed forms, based on psychomotor behavior. As an acute confusional state, it is characterized by a rapid onset of symptoms, fluctuating course and an altered level of consciousness, global disturbance of cognition or perceptual abnormalities, and evidence of a physical cause. Although pathophysiological mechanisms of delirium remain unclear, current evidence suggests that disruption of neurotransmission, inflammation, or acute stress responses might all contribute to the development of this ailment. It usually occurs as a result of a complex interaction of multiple risk factors, such as cognitive impairment/dementia and current medical or surgical disorder. Despite all of the above, delirium is frequently under-recognized and often misdiagnosed by health professionals. In particular, this happens due to its fluctuating nature, its overlap with dementia and the scarcity of routine formal cognitive assessment in general hospitals. It is also associated with multiple adverse outcomes that have been well documented, such as increased hospital stay, function/cognitive decline, institutionalization and mortality. In this context, the early identification of delirium is essential. Timely and optimal management of people with delirium should be performed with identification of any possible underlying causes, dealing with a suitable care environment and improving education of health professionals. All these can be important factors, which contribute to a decrease in adverse outcomes associated with delirium.

Keywords: delirium, aged, diagnosis, etiology, prevention and control

INTRODUCTION

The word delirium is derived from the Latin term *delirare*, meaning to become "crazy or to rave" (Saxena and Lawley, 2009). It has been documented in medical literature for more than 2000 years, with a fairly consistent clinical description (Adamis et al., 2007). It was reported during the time of Hippocrates, who used the words *phrenitis* (frenzy) and *lethargus* (lethargy) to describe the hyperactive and hypoactive subtypes of delirium. As a medical term, delirium was first used by Celsus in the first century A. D. to describe mental disorders associated with fever or head trauma (Khan et al., 2009).

A variety of terms have been used in the literature to describe delirium, including "acute confusional state," "acute brain syndrome," "acute cerebral insufficiency," and "toxic-metabolic encephalopathy" (Morandi et al., 2008). However, delirium is now the preferred term (Gill and Mayou, 2000) and it has been suggested that acute confusional state should be the only accepted synonym for this syndrome (Lipowski, 1992).

Delirium was standardized for the first time as a clinical entity in the Diagnostic and Statistical Manual of Mental Disorders, third edition/DSM-III (APA, 1980). The more recent version of this manual is now considered to be the gold standard for delirium diagnosis (CCSMH, 2006; NICE, 2010). Furthermore, this classification has been designed to be simple and sensitive enough to detect the presence of delirium in different settings, in particular among acutely ill and hospitalized elderly patients (Laurila et al., 2004).

According to the current DSM criteria (APA, 2000), delirium is characterized by the rapid onset of symptoms that tend to fluctuate even during the same day with an altered level of consciousness, global disturbance of cognition or perceptual abnormalities and evidence of a physical cause, substance intoxication/withdrawal, or multiple etiologies.

Delirium is a common and serious problem, mainly in hospitalized elderly patients (Saxena and Lawley, 2009). Its diagnosis is based on clinical history, key features observation, and physical and cognitive assessment (Fearing and Inouye, 2009; Fong et al., 2009a).

The etiology of delirium is usually multifactorial, resulting commonly from a combination of predisposing and precipitating factors (Rolfson, 2002; CCSMH, 2006). Its pathophysiological mechanisms remain poorly understood, with some evidence for the contribution of neurotransmission disruption, inflammation, or acute stress responses (Saxena and Lawley, 2009).

Delirium has also been associated with multiple adverse outcomes (Siddiqi et al., 2006; Cole et al., 2009). It is often poorly diagnosed, in particular due to its fluctuating nature, its overlap with dementia and lack of formal cognitive

assessment in general hospitals (Cole, 2005; CCSMH, 2006; Inouye, 2006).

In the management of delirium, non-pharmacological interventions have been considered the first-line strategy (Fong et al., 2009a), which includes, initially, the identification of underlying causes, supportive care (with involvement of family), and manipulation of the environment. In spite of that, prevention strategies emerge as the most important and cost-effective approaches for delirium, contributing to the decrease in its frequency, and associated poor outcomes (Inouye, 2006; NICE, 2010), namely in patients with Alzheimer's disease (Fick et al., 2002), given the evidence that delirium accelerates disease progression, even in cases where the etiology does not involve any cerebral structural insult.

EPIDEMIOLOGY

Delirium is a common and serious condition among the elderly, particularly in hospitalized patients, affecting up to 30% of this patient population (Saxena and Lawley, 2009). Most recent studies report a prevalence of delirium of 10–31% on admission and an incidence of 3–29% during hospitalization (Siddiqi et al., 2006).

This risk increases exponentially in intensive care units, with prevalence rates of up to 80% (Morandi and Jackson, 2011) and in palliative care units, where it is reported to be as high as 85% (Casarett and Inouye, 2001). Higher rates are also noted in surgical settings (Young and Inouye, 2007), with an incidence reported to range from 10 to 70% after surgery (Guenther and Radtke, 2011), especially in patients undergoing cardiothoracic surgery, emergency orthopedic procedures (repair of a hip fracture), vascular surgery, or cataract removal (Saxena and Lawley, 2009). Studies among elderly people presenting in emergency departments have reported prevalence rates of 5–30% (Lewis et al., 1995; Elie et al., 2000; Inouye, 2006).

In spite of long-term care, nursing home residents represent a vulnerable group, but only a few studies have been carried out (CCSMH, 2006). In a recent study (McCusker et al., 2011) the prevalence of delirium has been estimated between 3.4 and 33.3%. In the community, as expected, the prevalence is lower, ranging from 1 to 2% (Popeo, 2011).

CLINICAL FEATURES

Based on DSM-IV-TR criteria, delirium is characterized by the rapid onset of symptoms (usually hours or days) and tends to fluctuate, with an altered level of consciousness, with an inability to focus, sustain or shift attention, and a change in cognition (such as memory impairment, disorientation, language disturbance) or development of a perceptual disturbance that is not better accounted for by dementia. Moreover, there is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition, or substance intoxication/withdrawal, or due to multiple etiologies (APA, 2000).

This definition has the advantage of covering a broad clinical spectrum, but it also implies great complexity. The areas of neurological function identified are indeed wide and can hardly be attributed to the activity of discrete cerebral structures. Also controversial is the interpretation that the syndrome is caused by the ability of different etiological factors to impact on a final common pathway producing stereotyped clinical consequences (Caraceni and Grassi, 2011).

Sudden and acute onset and fluctuating course are the central features of delirium. Therefore, it is important to establish the patient's level of baseline cognitive functioning and the course of cognitive change (Fearing and Inouye, 2009). Symptom fluctuation is unpredictable. They may be intermittent, and are often worse at night (Cole, 2004).

Consciousness as a brain function allows the awareness of oneself and of the environment (Fish, 1967) and is characterized by two main aspects: the level of consciousness and the content of consciousness (Plum and Posner, 1972). The level of consciousness reflects arousal and vigilance: being awake, asleep, or comatose. The content of consciousness, or part of it, is experienced by the subject as awareness of him or herself and of the environment when awake and normally alert. The content of consciousness and cognition can be examined only if at least a certain degree of wakefulness and alertness are preserved (Caraceni and Grassi, 2011).

Consciousness should also be considered as a continuum from full alertness and awareness to coma and its impairment appears as the primary change in acute organic disorders. In this sense, it places an important role in the detection of acute disturbances of brain function, as well as, in the assessment of its severity (Lishman, 1997).

In delirium, the disturbance of consciousness is one of the earliest manifestations, which often fluctuates, mainly in the evening when environmental stimulation is at its lowest (Burns et al., 2004). The level of consciousness may fluctuate between extremes in the same patient, or alternatively may present with more subtle signs, such as mild drowsiness, or an impaired level of attention (Saxena and Lawley, 2009). In fact, the patient may appear obviously drowsy, lethargic, or even semi-comatose in more advanced cases. The opposite extreme, hyper-vigilance, may also occur, especially in cases of alcohol or sedative drug withdrawal (less common in elderly people; Francis and Young, 2011).

Attention is the process that enables one to select relevant stimuli from the environment, to focus and sustain behavioral responses to such stimuli, and to switch mental activity toward new stimuli, reorienting the individual behavior, according to the relevance of the stimulus (Caraceni and Grassi, 2011). Attention is a different function from consciousness, but it is dependent on it. Thus, variable degrees of attention are possible with full consciousness, but complete attention and concentration are impossible with diminished consciousness. In fact, attention may be pathologically decreased in organic states, usually with lowering of consciousness (Oyebode, 2008).

In delirium, inattention occurs and it is also considered one of the important cardinal features (Cole, 2005). Usually these patients are easily distractible by irrelevant stimuli, or have difficulty keeping track of what was being said during the clinical interview. Moreover, most of the time, the questions must be repeated because the individual's attention wanders (APA, 2000).

Typically there are global or multiple deficits in cognition, including memory impairment and disorientation. In fact, due to this inattentiveness, the registration of new information can be impaired, affecting memory, and orientation functions (Cole, 2004).

In the first case, the short-term memory is the most commonly affected (APA, 2000; Longo et al., 2011), but retrieval of stored information can also be disturbed (Saxena and Lawley, 2009). For instance, patients can have an inability to remember events in the hospital or difficulty in remembering instructions (Inouye, 2003).

Disorientation is usually common, first in reference to time and then to place (Burns et al., 2004). However, it may be considered not abnormal for an inpatient that has been seriously ill for a long time, without references of days or months.

The functions of thinking and speaking overlap and cannot be readily separated from each other, but they are clearly different. Both can be impaired in delirium (Oyebode, 2008).

Language difficulties and its impoverishment in delirium patients are probably more related to the disorder of arousal and attention levels, than a specific cause, or still they may reveal a thought process alteration. In severe cases of global impairment, frank confabulation can dominate, leaving little opportunity to assess language, memory, and thought content. Often language and speech, including reading, are less affected than writing, especially in mild or early stages. Few specific observations on language disturbances found in the course of delirium are available. In one study, misnaming has been commonly found, as frequent as observed in demented patients, but they differed in being more often of the types of word intrusion and unrelated misnaming (Wallesch and Hundsaltz, 1994). Word intrusion is in part explained by perseveration. The patient repeats a previously uttered word (therefore perseverating) rather than the expected word that he/she is unable to find or pronounce. Unrelated misnaming is the use of word that wildly differs in meaning from the intended word and therefore has no relationship with the word appropriate for the context, unlike paraphasia (Caraceni and Grassi, 2011).

Another clinical feature is disorganized thinking, manifested by incoherent speech and rambling or irrelevant conversation, or unclear or illogical flow of ideas (Inouye, 2006). The patient may be unable to make appropriate decisions, or execute simple tasks. Their judgment and insight may be poor and delusions can also occur in around 30% of the cases (Meagher et al., 2007), particularly of a paranoid or persecutory nature (Cole, 2004).

Perceptual disturbances have also been described in people with delirium. These may include illusions and misinterpretations, which arise from a false impression of an actual stimulus. For example, a patient may become agitated and fearful, believing that a shadow in a dark room is actually an attacker. The perceptual disturbance can also include hallucinations, where no object is actually present (Oyebode, 2008). Visual hallucinations are the most frequent, often occurring at night (Cole, 2004), and in some cases they can appear during the day as soon as the patient closes his eyes. The content of the hallucinations tends to be simple, at times just colors, lines, or shapes (Caraceni and Grassi, 2011). However, it can include, for instance, dangerous animals or bizarre images (Saxena and Lawley, 2009).

There are other clinical features commonly associated with delirium that are not included in the diagnostic criteria (Fearing and Inouye, 2009). One of them is sleep-wake cycle disturbance, characterized by an excessive daytime sleepiness with insomnia at night, fragmentation, and reduction of sleep or complete sleep-cycle reversal (Inouye, 2006).

Some studies have observed the potential role of these disturbances, in particular disordered circadian rhythm (Bachman and Rabins, 2006) and sleep fragmentation (Kim et al., 2005) as an important contributing factor to the sundowning syndrome. This phenomenon has been seen in patients with delirium and is characterized by worsening of disruptive behavior in the late afternoon or evening. This syndrome may also be due to fatigue and reduced sensory input toward the evening (Bachman and Rabins, 2006; Saxena and Lawley, 2009).

Disturbed psychomotor behavior is another clinical feature of delirium, with unusually increased or decreased motor activity. In the first case, patients may have restlessness or frequent sudden changes of position. On the other hand, the patient may also show sluggishness or lethargy, approaching stupor (APA, 2000).

In these patients, emotional disturbances, such as anxiety, fear, irritability, anger, depression, and euphoria, may also be seen. These symptoms are often influenced by factors, such as medical or surgical conditions, personality characteristics, premorbid psychiatric disorders, or recent life events (Cole, 2004).

According to some authors (Meagher et al., 2008) some caveats should be taken into account in the discussion of delirium classification and criteria currently used.

For instance, despite the tendency to make the criteria explicit according to the specificity of the symptoms of delirium, it must be remembered that certain clinical situations, hospitalization, or physical symptoms, such as pain or breathing difficulty, can give rise to pseudo-delirious symptoms, such as sleep disturbance (Caraceni and Grassi, 2011).

Moreover, a poor correlation has been shown between the different sets of diagnostic criteria (DSM-IV, ICD-10). In particular, a study (Laurila et al., 2003) reported different delirium prevalence rates in elderly people admitted to hospital or nursing homes, according to the criteria used (24.9% by DSM-IV and 10.1% by ICD-10). These results clearly indicate that too inclusive or too restrictive criteria can cause marked differences in estimated prevalence rates of delirium (Caraceni and Grassi, 2011).

Bearing this controversy in mind, some authors (Watt et al., 2012) go beyond this criticism of delirium in the DSM-IV criteria. These authors have questioned the notion of delirium as reflecting an "altered level of consciousness." As an alternative, these authors have suggested that delirium reflects the collapse of cognitive operations (attention, working memory, and executive functions), in direct proportion to the severity of any confusional state, and given that these processes are basilar for every other cognitive process, their breakdown compromises the entire cognitive apparatus (Watt et al., 2012). These processes define a base for the cognitive pyramid and are functionally deeply interdigitating, and difficult to neatly separate (Watt and Pincus, 2004). This perspective is not present in the current DSM criteria.

Another limitation is related to the severity of delirium, which is inadequately represented in this classification, as the complete clinical spectrum ranges from very severe deliriums where patients are minimally conscious, to low-grade encephalopathic states in a broad continuum, frequently missed by clinicians (Watt et al., 2012).

So, according to these authors (Watt et al., 2012), delirium might belong to a broader category of diseases of consciousness. They have suggested the following as a rough heuristic, with disorders of consciousness ranging from the most severe to the least severe: Coma; Persistent Vegetative State; Stupor; Akinetic Mutism; Minimally Conscious State; Delirium/Confusional States (Watt and Pincus, 2004). Such taxonomy would provide a continuum, with "gray zones," or transitional regions demarcating one disorder from the next. This approach would further allow for a continuum of severity in relation to delirium itself, which is currently disregarded in DSM-IV (Watt et al., 2012).

In spite of this, clinical evaluation according to the symptom phenomenology and the nosographic criteria appears as a reference standard for the diagnosis of delirium. In addition, the correct examination of delirious symptoms for epidemiological reasons, research, and clinical purposes is essential and has been reported by many authors (Casarett and Inouye, 2001; Breitbart et al., 2009).

SUBSYNDROMAL DELIRIUM

Since the publication of well-established sets of diagnostic criteria, such as the DSM-IV, there has recently emerged a new concept known as subsyndromal delirium (Voyer et al., 2009).

This condition has been defined as the presence of one or more core diagnostic symptoms that do not meet the full criteria for delirium, and where progression to delirium does not occur. The core symptoms were: inattention, altered level of consciousness, disorientation, and perceptual disturbances (Levkoff et al., 1996; Cole et al., 2003).

From a clinical perspective, some authors have suggested an alternative term: "low-grade confusional state." This emphasizes the need to rate the severity of confusional states – mild, moderate, severe – in opposition to the strict concept of DSM-IV (Watt et al., 2012). As suggested by Voyer et al. (2009), these criteria, when applied very literally, produce underestimation of delirium.

Subsyndromal delirium occurs in 21–76% of hospitalized elderly people (Cole et al., 2008). Prevalence rates of 30–50% have been reported in intensive care units (Ouimet et al., 2007). In long-term care elderly residents, with dementia, the occurrence was 48.4 or 50.3%, depending on the criteria used (Voyer et al., 2009). A recent cohort study has found that 68 of the 104 residents had incident subsyndromal delirium during 6 months of observation. The incidence rate was 5.2 per 100 person-weeks of follow-up (Cole et al., 2011).

The risk factors for subsyndromal delirium are similar to those for classical overt delirium: advanced age, dementia, and severe illness. Moreover, this condition has been associated with poor outcomes, such as a lower cognitive and functional level, increased length of acute care hospital stay, and decreased post-discharge survival at 12 months (Cole et al., 2003).

Thus, patients with subsyndromal delirium require identification and clinical attention in line with management of delirium in order to attain the best outcome (Levkoff et al., 1996).

CLINICAL SUBTYPES

Lipowski (1980) was the first author to suggest that delirium can occur in three clinical forms: hyperactive, hypoactive, and mixed, based on psychomotor behavior. This classification is not recognized by DSM-IV or ICD-10 (International Classification of Diseases; WHO, 1992) diagnostic criteria (Lindsay et al., 2002). However several studies have confirmed the existence of this clinical classification (Camus et al., 2000; de Rooij et al., 2005).

In the hyperactive subtype, there is increased psychomotor activity. Patients show features such as hyper-vigilance, restlessness, agitation, aggression, mood lability, and in some cases, hallucinations and delusions (Lipowski, 1980). Behaviors are frequently disruptive (e.g., shouting or resisting, pulling out the IV tubing) or potentially harmful (e.g., pulling out catheters). Because of this, this subtype is the most easily identified (Saxena and Lawley, 2009). Moreover, patients with this form are more likely to be medicated, in particular with benzodiazepines and neuroleptics (Caraceni and Grassi, 2011).

In contrast, the hypoactive form is characterized by decreased psychomotor activity, with the presence of lethargy and drowsiness, apathy, and confusion. Patients become withdrawn, answering slowly to questions and without spontaneity. Sometimes patients can also appear to be sedated (NICE, 2010). This is the most common subtype of delirium in elderly people (Meagher et al., 2011). In a recent study (Khurana et al., 2011) with hospitalized elderly delirious patients, a high prevalence of hypoactive delirium was found (65%), when compared to the other forms. However, due to the absence of disruptive and injurious behaviors, this subtype can be more difficult to recognize by clinicians (NICE, 2010; Mittal et al., 2011).

In mixed delirium, patients have symptoms of both the subtypes mentioned above (Liptzin and Levkoff, 1992). It has been reported to be the most common type.

Different patterns have been suggested for these three different forms of delirium. Dissimilar underlying pathogenetic pathways will determine different management, course, prognosis, and outcomes (Meagher et al., 2000; de Rooij et al., 2005; Fong et al., 2009a).

Unfortunately, the literature is inconsistent about which subtype has the worse prognosis. However, some authors have suggested there is evidence that the hypoactive form is associated with a relatively poorer prognosis (Yang et al., 2009) and in a recent longitudinal study (Meagher et al., 2011), the patients with this subtype have been significantly more likely to die within 1 month of study entry.

DIAGNOSIS

Delirium is frequently under-recognized and often misdiagnosed by health professionals. Between a third and two-thirds of delirium cases go unrecognized (Siddiqi et al., 2006). A recent study (Han et al., 2009) in an emergency department concluded that the emergency physicians missed delirium in 76% of the cases.

This under-recognition has been associated with factors such as the fluctuating nature of delirium, its overlap with dementia and depression, the scarcity of formal cognitive assessment in general hospitals by routine, under-appreciation of its clinical consequences, and failure to consider the diagnostic importance (CCSMH, 2006; Inouye, 2006; Philpot, 2011). Non-detection of delirium has been also associated with the high prevalence of the hypoactive form of delirium (Armstrong et al., 1997). Four independent risk factors for the under-recognition of delirium by

nurses have been identified: hypoactive delirium, advanced age, vision impairment, and dementia (Inouye et al., 2001).

A recent survey of trainee physicians in the UK revealed a lack of basic knowledge about the diagnosis and management of delirium, although they appeared to be aware of its high prevalence in hospitals as well as its potential clinical significance (David and MacLullich, 2009).

The diagnosis of delirium remains primarily clinical, without specific diagnostic tests (Young and Inouye, 2007). In this way, it is made on the basis of clinical history, behavioral observation of key features, and comprehensive physical and cognitive assessment (Fearing and Inouye, 2009; Fong et al., 2009a). In this context, understanding and considering its clinical features is crucial for a correct diagnosis (Inouye, 2006).

Taking into account the acute onset and fluctuating course of delirium, it is important to establish the patient's level of baseline cognitive functioning and the course of cognitive change. In this way, the diagnosis is made more easily if there has been a prior assessment of cognitive abilities. In other instances it is necessary, in a clinical interview, to obtain information from the family members/caregivers and/or medical and nursing staff (Cole, 2005; Fearing and Inouye, 2009). Moreover, patients should be assessed more than once during the day, in order to detect a possible fluctuating path of symptoms.

Inattention is another central feature of delirium. The cognitive assessment should include not only global cognitive screening tools (e.g., Mini-Mental State Examination – MMSE; Folstein et al., 1975), but also a measurement of attention (Fearing and Inouye, 2009). There are quick screening instruments for inattention that are commonly used: Digit Span Test (Wechsler, 1997) and Trail Making Test A (Reitan, 1958). In this context, it is also important to note that changes in arousal can affect performance in attention tests as can other conditions, such as fatigue. Moreover, depending on the severity of delirium, cognitive tasks can be affected proportionally to attention demands required by the task (Oyebode, 2008).

The level of consciousness is another important aspect of this evaluation that has to be determined. The Glasgow Coma Scale (Teasdale and Jennett, 1974) has been classically used to quantify this level of consciousness.

According to the most recent international guidelines (NICE, 2010), all elderly people admitted to hospital or in long-term care units should be screened for risk factors of developing delirium and cognitive impairment, using a brief cognitive test (e.g., MMSE). If recent changes or fluctuations in cognitive function, perception, physical function, or in social behavior are identified in people at risk, a clinical assessment should be carried out based on the DSM-IV criteria or short Confusion Assessment Method – CAM (Inouye et al., 1990), CAM (algorithm) to confirm the diagnosis. This evaluation should also be carried out by a trained healthcare professional.

The CAM is a widely used delirium screening instrument, based on DSM-III-R criteria (APA, 1987). It can be readily used in routine clinical settings by non-psychiatric medical or nursing staff with some previous training (Wei et al., 2008). The short version includes a diagnostic algorithm, based on four cardinal features of delirium: (1) acute onset and fluctuating course; (2) inattention; (3) disorganized thinking; and (4) altered level of consciousness. A diagnosis of delirium according to the CAM requires the presence of features 1, 2, and either 3 or 4. In critical care or in the recovery room after surgery, in particular in patients who are not able to communicate verbally, CAM-ICU (Ely et al., 2001), an adaptation derived from CAM, should be used (Luetz et al., 2010; NICE, 2010). Recent review studies (Adamis et al., 2010; Wong et al., 2010) corroborated this recommendation, citing evidence to support the use of CAM as a diagnostic instrument. The use of the Delirium Rating Scale-R-98 – DRS-R-98 (Trzepacz et al., 2001) has also been suggested as a measure of delirium symptom severity in effective assessment. This scale includes three diagnostic items (onset, fluctuation of symptoms, physical disorder) and 13 severity items (sleep-wake cycle, perceptual disturbances/hallucinations, delusions, lability of affect, language, thought process abnormalities, motor agitation, motor retardation, orientation, attention, short-term memory, long-term memory, visuospatial ability). A high score is indicative of greater severity.

The identification of underlying causes is crucial in delirium diagnosis (Marcantonio, 2011). Because of that, physical and neurological examinations are extremely important, helping to rule out infectious, metabolic, endocrine, cardiovascular, and cerebrovascular diseases (Fong et al., 2009a).

The diagnostic approach should include the following tests: complete blood count, blood urea and creatinine levels, electrolytes, blood sugar, C-reactive protein, liver function, and thyroid function (Cole, 2004; Saxena and Lawley, 2009).

It is also important to identify medication and substance usage, namely alcohol or benzodiazepines use, which can contribute to this ailment (Inouye, 2006).

The physical examination should also include the evaluation of vital signs, with oxygen saturation. The general examination should focus on cardiac and pulmonary function. Beyond this, a neurological examination should incorporate the mental status, as well as focal findings (Marcantonio, 2011).

No laboratory test, brain imaging or other tests are more accurate than clinical assessment (Inouye, 2006). However, they can be useful to identify possible causes of delirium and correctable contributing factors. In some situations, brain imaging and electroencephalography (EEG) can be useful, when there is strong evidence of an intracranial cause, based on clinical assessment (e.g., change in mental status after a blow to the head) or if focal neurological signs or seizure activity is detected during physical examination (Hirano et al., 2006; Saxena and Lawley, 2009).

DIFFERENTIAL DIAGNOSIS

Delirium is frequently confused with dementia (**Table 1**). Globally, dementia is characterized by cognitive and functional impairment and usually follows a chronic deteriorating course, whereas delirium is characterized primarily by inattention and has an acute onset with a fluctuating course (Meagher et al., 2006). Also, an abnormal level of consciousness is highly suggestive of delirium, while in dementia attention and the level of consciousness tend to remain intact (Fearing and Inouye, 2009; Marcantonio, 2011), at least until late stages, or in the case of Dementia with Lewy Bodies (DLB; McKeith et al., 2005).

Table 1 | Differential diagnoses of delirium and dementia.

	Delirium	Dementia
Onset	Acute	Insidious
Duration	Hours, days, months	Months to years
Course	Fluctuating (often worse at night)	Chronic, progressive (but stable over the course of the day, except for DLB)
Consciousness	Altered (hyperalert, alert, or hypoalert)	Alert
Attention	Impaired	Normal (except in late stages)
Memory	Impaired (registration, recent, and remote)	Impaired (recent and remote)
Orientation	Usually impaired	Often impaired
Speech	Often incoherent, slow, or rapid	Coherent (with mild errors) until the late stage
Thinking	Disorganized or incoherent	Impoverished and vague
Perception	Altered	Altered or normal
	Hallucinations are frequent (mainly visual)	Hallucinations often absent (except in advanced stages or DLB)

Additionally, physical illness or drug toxicity can alone or together be present in delirium, whereas it is often absent in Alzheimer's disease (Saxena and Lawley, 2009).

Although delirium and dementia are often separated clinically and methodologically, these conditions often occur together, with prevalence ranges from 22 to 89% in both hospital and community settings. These clinical situations are also probably highly interrelated, specifically because both share many pathophysiological features (Fick et al., 2002, 2009).

Delirium complicates 24–89% of inpatient stays for elderly patients with dementia (Sampson et al., 2009). Inversely, the available evidence strongly suggests that delirium increases the risk of new-onset dementia in the long-term, as much as sixfold at 3 year follow-up (MacLullich et al., 2009). Also, people with pre-existing dementia suffer from an acceleration of cognitive decline following an episode of delirium (Fong et al., 2009b).

However, distinguishing delirium and dementia becomes crucial because the diagnosis of delirium is urgent, as it can be the first indicator of a serious medical problem (Wahlund and Bjorlin, 1999), which can be treatable, and because it has been associated with poor outcomes (Siddiqi et al., 2006).

Differential diagnosis with DLB can also be difficult. In both clinical situations, there is a fluctuating course, altered level of consciousness, as well as visual hallucinations. However, this type of dementia has a longer duration (months or years) and parkinsonian symptoms are common (McKeith et al., 2005). Besides, visual hallucinations are more complex and persistent in DLB than in delirium (Cole, 2005).

Depression may also be mistaken for the hypoactive form of delirium, due to the presence of symptoms such as slowed thinking, decreased concentration, and memory impairment. However, the presentation of depression tends to be insidious, without fluctuations and the level of consciousness remains unaffected. Moreover, there is usually a history of previous episodes, and a predominance of mood symptoms (Cole, 2005; Saxena and Lawley, 2009).

Other less common situations should also be considered, such as mania and schizophrenia (Saxena and Lawley, 2009). In the first case, it can be confused with the hyperactive form of delirium, with reduced attention, agitation, and rapid fluctuations. However, in this situation there are usually previous episodes of euphoria/mania (Cole, 2005).

In the second case, disturbance of thought can be also present in both. However, in delirium, these alterations fluctuate and are often fragmentary and less complex. Thought insertion, very common in schizophrenia, is unusual in delirium. On the other hand, schizophrenic delusions are very systematized, bizarre, and not influenced by the environment, which contrasts with the poor systematization and environmental influence observed in delirium (Cole, 2005).

Perception is also affected in schizophrenia, with hallucinations. They are persistent, consistent, and usually auditory, as opposed to those occurring in delirium, which are predominantly visual (Saxena and Lawley, 2009).

PATHOPHYSIOLOGY

The pathophysiological mechanisms of delirium remain unclear (Gofton, 2011). However, current evidence suggests that disruption of neurotransmission can contribute to the development of this disorder (Saxena and Lawley, 2009).

The neurotransmitter hypothesis suggests that cholinergic deficits and dopaminergic excess could be involved in the development of delirium (Trzepacz, 2000; Gaudreau and Gagnon, 2005). Indeed, the cholinergic system has an important role in cognition and attention (Hshieh et al., 2008), so its impact in the development of delirium is not surprising. Moreover, drugs with anticholinergic properties may precipitate delirium, in susceptible individuals (Trzepacz, 1996). There is also strong evidence supporting the importance of the role of cholinergic deficits in the development of this condition (Gofton, 2011).

Another important neurotransmitter that could be involved in delirium is dopamine, since delirium can be a common side effect of the dopaminergic drugs used in the treatment of Parkinson's disease (Trzepacz and van der Mast, 2002). This neurotransmitter has been related to psychotic symptoms (Ramirez-Bermudez et al., 2008), which can reinforce the function of these symptoms in delirium, if not the whole syndrome (Hall et al., 2011). Furthermore, dopamine also has an important role in motor activity, as well as, cognitive functions, such as attention, thought, and perception (Trzepacz, 2000), which are affected in this clinical condition.

Inflammation or acute stress responses are less supported pathophysiological mechanisms (Fong et al., 2009a). The first has been inferred from basic and clinical research literature evidence, supporting the hypothesis that trauma and infection or surgery can lead to increased production of cytokines (Rudolph et al., 2008; Cerejeira et al., 2010). This mechanism may induce delirium in susceptible patients (Maclullich et al., 2008). Furthermore, a recent review concluded that this increase in cytokines plays a crucial role, specifically in the development of cognitive dysfunction, observed in delirium (van Munster et al., 2008; Simone and Tan, 2011).

On the other hand, a recent prospective study (Cerejeira et al., 2011) stated that elective hip-replacement surgery induced a reduction of plasma activity of cholinesterases (acetylcholinesterase – AChE and butyrylcholinesterases – BuChE) and found lower preoperative activity levels of plasma cholinesterases in subjects who developed delirium postoperatively.

Another hypothesis is related to cortisol, a hormone of the hypothalamic-pituitary-adrenal axis, which is part of the body's major response to stressful or traumatic insults (Olsson, 1999). Aging and dementia have been connected with an increase and duration of cortisol response to stress (MacLullich et al., 2008). This could explain why high levels of this hormone associated with acute stress have been hypothesized to precipitate and/or sustain delirium (Trzepacz and van der Mast, 2002).

Some authors (Watt et al., 2012) have suggested a simple heuristic that all etiologies for delirium emerge due to the deleterious effect of insults on neural networks supporting large-scale and highly integrative global cognitive processes involved in attention, working memory, and executive functions, which depend on the functional integrity of cortical prefrontal and parietal networks, as well as specific subcortical structures, such as the basal ganglia, cerebellum, thalamic nuclei, and the reticular activating system.

According to these authors, "a true understanding of delirium cannot emerge through simply focusing on single molecules, however important those particular transmitter systems may be, but can only come from focusing on the large-scale networks that underlie organized behavior and thought" (Watt et al., 2012).

RISK FACTORS

The etiology of delirium is usually multifactorial. However, it can be caused by a single factor, such as alcohol withdrawal or substance abuse (Burns et al., 2004; Fearing and Inouye, 2009).

Research has identified several consistent risk factors for delirium, which are classified into two groups: predisposing and precipitating factors. The first one makes the elderly person more vulnerable to the development of delirium and the second comprises acute factors for triggering delirium (CCSMH, 2006). A combination of these predisposing and precipitating factors appears to be the rule rather than an exception in delirious elderly people (Inouye, 1999; Rolfson, 2002).

The most common predisposing factors are: advanced age, male gender, pre-existing dementia and depression, visual and hearing impairment, functional dependence, dehydration and malnutrition, polymedication (mainly psychoactive drugs), alcohol abuse and coexistence of multiple, and severe medical conditions (Saxena and Lawley, 2009).

Next to increasing age, dementia appears as the second most frequent risk factor for delirium (Burns et al., 2004; Cole, 2004; CCSMH, 2006; Inouye, 2006). According to Inouye (2006), the underlying vulnerability of the brain in patients with dementia may predispose them to the development of delirium, as a consequence of insults related to the acute medical disease, medication, as well as environmental factors.

According to Saxena and Lawley (2009), the most common precipitating factors are: intercurrent illnesses (e.g., infections), iatrogenic complications, metabolic derangements, primary neurological conditions (e.g., acute stroke), surgery, drugs (particularly benzodiazepines, narcotic analgesics, and drugs with anticholinergic effects (Han et al., 2001). Uncontrolled pain has also been associated with the development of delirium.

Environmental factors, such as admission to an ICU, use of physical restraints or bladder catheterization have also been implicated (Brauer et al., 2000; Rolfson, 2002; Cole, 2004; Fong et al., 2009a; Saxena and Lawley, 2009).

In this context, Inouye and Charpentier (1996) present a model to predict the development of delirium in elderly hospitalized patients, with a greater number of or more severe predisposing factors (use of physical restraints, malnutrition, more than three medications in the previous day, use of a bladder catheter, and any iatrogenic event), in association to few precipitating factors. This model has been considered an excellent framework for identification of various etiologies of delirium in old age (Rolfson, 2002).

More recently, the guidelines (NICE, 2010) recommend the identification, in elderly people admitted to hospital or in long-term care, of the following risk factors: age 65 years old or over, cognitive impairment (past or present), dementia or both, current hip fracture, and presence of a severe illness. This identification brings the opportunity to change the risk factors for the development of delirium.

PROGNOSIS

Delirium in both medical and surgical elderly hospitalized patients has been associated with multiple adverse outcomes that have been well documented (NICE, 2010).

Overall, delirium has been associated with the increase of hospital stay (Cole and Primeau, 1993; Dubois et al., 2001; McCusker et al., 2003; Koster et al., 2011; van den Boogaard et al., 2011; Shi et al., 2012), cognitive decline (Inouye et al., 1998; McCusker et al., 2001; Jackson et al., 2004; Fong et al., 2009b; Witlox et al., 2010), functional decline (Inouye et al., 1998; Marcantonio et al., 2000; McCusker et al., 2001, 2002a), institutionalization (Cole and Primeau, 1993; Inouye et al., 1998; Witlox et al., 2010), and mortality (Cole and Primeau, 1993; Cole et al., 2008; Inouye et al., 1998; McCusker et al., 2002b; Witlox et al., 2010; Koster et al., 2011; Shi et al., 2012).

In intensive care units, delirium has been shown to be associated with prolonged duration of mechanical ventilation (van den Boogaard et al., 2011), longer stay in hospital, and in the ICU (Dubois et al., 2001; van den Boogaard et al., 2011) as well as mortality during hospitalization (van den Boogaard et al., 2011).

A systematic review (Siddiqi et al., 2006), with medical elderly in patients, concluded that this condition had been related to an

increase of mortality (discharge/12 months), length of hospital stay, and institutionalization.

More recently, a meta-analysis (Witlox et al., 2010) confirms that delirium is associated with the increased risk of dementia, institutionalization, and mortality, independently of important confounder factors (age, gender, comorbidity, severity of illness, and baseline dementia).

Fong et al. (2009b) demonstrate that incident delirium accelerates the trajectory of cognitive decline in hospitalized elderly patients with Alzheimer's disease.

Although traditionally viewing delirium as a transient and reversible condition, some studies have found evidence that a significant proportion of patients do not recover from delirium, presenting persistent symptoms at time of discharge, or beyond (Levkoff et al., 1992; Murray et al., 1993; McCusker et al., 2002b; Siddiqi et al., 2006; Cole et al., 2009). According to Cole et al. (2009), this situation, called persistent delirium, may contribute to the poor prognosis of delirium. These patients have worse outcomes (mortality, nursing home placement, function, and cognition), when compared with patients who have recovered from delirium (Cole et al., 2009; Cole, 2010). In a recent systematic review (Dasgupta and Hillier, 2010) persistent delirium was associated with dementia, medical conditions, severity of delirium, hypoactive symptoms, and hypoxic illness.

PREVENTION

Due to the adverse outcomes and increased health care costs that accompany delirium, the interventions to prevent this condition become crucial for reducing its frequency and complications (Inouye, 2006). In fact, one-third of delirium episodes could be prevented (Inouye, 2006; Marcantonio, 2011). Beyond that, the most recent guidelines (NICE, 2010) have considered delirium prevention as a cost-effective strategy. These provide a quick reference guide for preventing delirium in elderly people at risk, based on a multicomponent and non-pharmacological intervention that addresses a number of modifiable risk factors. First of all, people at risk of developing delirium (advanced age, suffering from cognitive impairment/dementia, hip fracture, or severe illness) should be assessed within 24 h of admission. In this case, the following 10 precipitating factor groups should be taken into consideration: cognitive impairment and disorientation, dehydration, and constipation, hypoxia, immobility/limited mobility, infection, polymedication, pain, poor nutrition, sensory impairment, and sleep disturbance. Based on this assessment, a trained and multidisciplinary team should provide a multicomponent intervention, taking into account the needs of the person, as well as the clinical care setting.

The success of a multidisciplinary and multicomponent approach in prevention of delirium springs from the many causes in the origin of this condition (Inouye, 2006; Fearing and Inouye, 2009; Salawu et al., 2009).

One of the most important examples of this kind of intervention was the Hospital Elder Life Program – HELP (Inouye et al., 1999, 2006), which was widely implemented (Marcantonio, 2011).

This intervention was carried out by a skilled interdisciplinary team and trained volunteers with standardized protocols for a personalized management of six risk factors (cognitive impairment, sleep deprivation, immobility, visual and hearing impairment, and dehydration). The effectiveness of this intervention decreased the incidence of delirium in 40% of cases and resulted in significantly fewer days and episodes of delirium.

On the other hand, educational programs targeting health professionals have been used alone or as part of multicomponent interventions, which seems to be crucial for a more appropriate management of patients with delirium (CCSMH, 2006), from the primary care level.

In regard to this, Naughton et al. (2005) have studied the effectiveness of multifactorial intervention designed to reduce delirium and hospital stay in elderly patients, carried out among a group of physicians and nurses from an emergency department and an acute geriatric unit. This intervention was shown to contribute to a decrease in psychotropic medication prescription (benzodiazepine and antihistamine), delirium prevalence, and hospital stay.

In another study (Tabet et al., 2005), an educational program for medical and nursing staff on an acute medical ward also contributed to a reduction in delirium prevalence in an intervention group, compared with a control group. Staff members were also more likely to correctly recognize this clinical condition.

In this context, a recent review (Teodorczuk et al., 2010) concluded that the majority of educational interventions focused on delirium prevention and management were shown to be effective in various healthcare settings. Moreover, this study also recognized that these programs should be carried out by a Liaison Old Age Psychiatry team, in particular in a hospital setting. This has been shown to be effective, with an improvement in key outcomes (Slaets et al., 1997).

MANAGEMENT

Once delirium occurs, non-pharmacological interventions should be considered as the first-line of delirium management (Cole, 2004; Fong et al., 2009a; Aguirre, 2010). This approach should address all evident causes, providing supportive care and preventing complications and treating behavioral problems (Inouye, 2006).

As delirium is a medical emergency and requires urgent intervention, the management of this condition must focus initially on identification and monitoring of underlying causes (CCSMH, 2006; NICE, 2010).

Supportive care remains as another important non-pharmacological strategy (Young and Inouye, 2007). This includes close and continuing observation and care from nursing staff, which should include vital sign monitoring, protecting the patient's airway, ensuring nutrition, correction and prevention of dehydration, attention to oral intake, prevention of aspiration, encouragement of mobility, and ensuring a good sleep pattern. In this context, it is also essential to support the patient's daily care and encourage self-care (Meagher et al., 1996; Cole, 2005; BGS, 2006; Inouye, 2006; Young and Inouye, 2007; Fearing and Inouye, 2009). The use of physical restraint is always questionable, but may be necessary to control violent behavior or to prevent the removal of important devices, such as endotracheal tubes (Marcantonio, 2011). However, it should be avoided, because it has been associated with worsening agitation and injury, prolonged delirium, and increased complications (Inouye, 2006; Young and Inouye, 2007).

Another important factor for the effective management of delirium is the involvement of the family and caregivers by health professionals. They can help re-orientate, calm, assist, protect, and support older people. Furthermore, they can also facilitate effective communication (CCSMH, 2006; NICE, 2010; Marcantonio, 2011). Medical and nursing staff, as well as families, should know the importance of effective communication in these situations. This can include strategies such as frequent verbal reorientation, clear instructions, and eye contact (Fearing and Inouye, 2009).

Delirium can be a psychologically traumatic experience, not only for the patients, but also for their family or caregivers (Breitbart et al., 2002). In this way, providing support and information can help throughout this process, as well as encouraging people to share their experiences (Inouye, 2006).

The education of families and caregivers by health professionals about delirium, in particular about its symptoms (especially disinhibition, agitation, hallucinations, and delusions) becomes crucial (CCSMH, 2006). It is also important to explain the fluctuating course, explaining that the transitory phases of awareness do not necessarily mean a recovery, because symptoms can recur. The possible causes of delirium, a possible relation with Alzheimer's disease or dementia, as well as treatment options should also be clearly explained. In fact, this specific intervention can be extremely important to the family, contributing not only to an improvement of their involvement in the management of delirium, but also to alleviate the profound sense of helplessness, incredulity, and anxiety that these members can feel during an episode of delirium (Gagnon et al., 2002).

Environmental manipulation is also recommended as an integral part of delirium management (NICE, 2010). It may include the following strategies: ensuring that there is a clock and a calendar in the room; giving the older person frequent verbal reminders of the time, day, and place; avoiding medical/nursing staff changes; transferring the patient to an isolated room, if possible; obtaining familiar possessions from home (e.g., family picture); avoiding sensory deprivation (e.g., windowless room) or sensory overload (e.g., too much noise); minimizing sensory impairment (including vision and hearing loss) by the use of corrective devices.

Pharmacological interventions in delirium should be considered only in the management of behavioral symptoms, but not for the basic treatment of this condition (Flaherty et al., 2011). They can be useful in situations of severe agitation, which interfere with medical procedures or when the patient puts himself or others, at risk and when non-pharmacological interventions fail (Inouye, 2006; NICE, 2010; Rathier and Baker, 2011).

In this context, the most recent guidelines (NICE, 2010) recommend the administration of haloperidol or olanzapine, only for a short period of time (for a maximum of 1 week or less), starting with low doses and titrating carefully, according to symptom severity.

In spite of this, the U.S. Food and Drug Administration has not yet approved any of these agents for the treatment of delirium (Flaherty et al., 2011).

With the use of antipsychotics one always has to take into consideration one of the most adverse effects of this high-potency medication: akathisia (motor restlessness), which can be confused with worsening of delirium (Marcantonio, 2011), or even being worse it in reality (Francis, 1992; Inouye et al., 2011). Recent evidence indicates that the use of antipsychotics is not safe in elderly patients, especially in those with dementia. Concerns include the development of adverse vascular events and death (Mittal et al., 2011).

On the other hand, the administration of antipsychotics should be avoided in Parkinson's disease or DLB (NICE, 2010).

Benzodiazepines have also been recommended, but only in delirium due to alcohol and benzodiazepine withdrawal, or neuroleptic malignant syndrome (Lonergan et al., 2009).

The introduction of cholinesterase inhibitors for the treatment of dementia suggested their potential usefulness to improve symptoms of delirium (Caraceni and Grassi, 2011). However, there is no specific evidence from controlled trials that donepezil or rivastigmine are effective in the treatment of this medical condition (Overshott et al., 2008; Gamberini et al., 2009).

The plan of discharge from hospital should be handled carefully, involving the team of health professionals and the patient, as well as the family (Saxena and Lawley, 2009). In addition, as symptoms of delirium can persist (Cole, 2010), a close clinical follow-up after discharge is crucial, especially due to the poor outcomes associated with this situation (BGS, 2006; Inouye, 2006). This could help identify residual cognitive, social, or functional problems, modify risk factors and help to reduce the recurrence of an episode of delirium (Saxena and Lawley, 2009).

CONCLUSION

Delirium is a common neuropsychiatric syndrome, mainly in elderly hospitalized patients. Despite this, it is frequently underrecognized by health professionals, due to its fluctuating nature, its overlap with dementia and the scarcity of formal cognitive assessment in general hospitals by routine. Once manifested, delirium is associated with increased morbidity and mortality. For that reason, prevention based on risk factor identification, early recognition, as well as an effective management, particularly if based on non-pharmacological strategies, is essential, because of the prevalence and the adverse outcomes associated with this disorder.

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Elderly Delirium Assessment Tools Review

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Abstract: *Background:* Delirium is a complex multifactorial neuropsychiatric disease, associated with negative outcomes: increased length of hospital stay, functional and cognitive decline, institutionalization and mortality. It is often poorly recognized due to its fluctuating nature, its overlap with dementia and the lack of valid and specific rating scales in clinical routine. *Aim:* This study review describes the characteristics and psychometric properties of delirium scales available in research and clinical practice. *Methods:* The MEDLINE database was used to identify the delirium scales (1990-2010), using keywords: delirium, confusion, severity, questionnaires, scales and screening. Only primary and validation studies were included. The exclusion criteria were children and alcohol or drug delirium assessment scales. *Results:* This study included seven screening scales (CAM, ICDSC, DSI, NEECHAM, CTD, DOSS, Nu-DESC) and six severity scales (DRS-98-R, MDAS, CSE, DSS, DI, DOM). The psychometric properties of each scale were reported. The majority of scales were based on the Diagnostic and Statistical Manual of Mental Disorders – DSM-IV criteria as well as on a review of selected symptoms of delirium informed by systematic clinical observation and formal brief assessment of mental status. *Conclusions:* The selection of instrument may be dependent on administration time and rater training requirements. However, bearing in mind the recent reviews included, the CAM is considered the most widely used instrument for delirium diagnosis and the DRS-98-R to measure the severity of delirium states. In overall studies these instruments revealed good psychometric properties: sensitivity/specificity (CAM 100-94%/95-90%; DRS-98-R 92%/93%) and interobserver reliability (CAM k=0.81-1; DRS-98-R ICC=0.98-0.99).

Keywords: Delirium, Elderly, Older assessment, Scales, Screening, Severity.

INTRODUCTION

Delirium (sometimes called 'acute confusional state') is characterized by the rapid onset of symptoms (usually hours or days) which fluctuate, with an altered level of consciousness and a change in cognition or development of a perceptual disturbance that is not better accounted for by dementia. There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition [1].

It is a common problem in the elderly, affecting up to 30% of all hospitalized older patients, increasing in surgical inpatients (hip fracture and vascular diseases), with an incidence varying between 5% to 35% [2].

Elderly people with previous cognitive decline or dementia, severe illness or a hip fracture are more at risk of developing delirium [3].

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Delirium is associated with multiple adverse outcomes that have been well documented, such as increased length of hospital stay, functional and cognitive decline, institutionalization and mortality [4, 5].

However, poor recognition remains the single greatest obstacle to both clinical and research efforts in delirium. This situation has been attributed to hypoactive delirium, older age, vision impairment, the overlap with dementia [6], the fluctuating nature of delirium, as well as the lack valid and specific rating scales as part of standardized operating procedure in clinical routine, mainly in populations at risk, in particular in elderly hospitalized patients, which is essential for early detection and timely management of delirium in this context [3, 7-9].

The DSM-IV [10] classification is considered to be the gold standard for diagnosis of delirium. It has also been shown to be particularly sensitive among acutely ill and hospitalized patients [11]. However, this takes time and needs clinical expertise [3]. Besides this, a formal assessment using this reference standard may imply an extensive clinical interview and a sequence of cognitive tests [12]. In this way, the use of rating scales as a part of standardized operating procedure in clinical routine can be helpful for early delirium diagnosis and measuring its symptom severity [7]. In this

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context, that could contribute to a decrease in multiple adverse outcomes associated with this clinical condition.

This study review describes the characteristics and psychometric properties (sensitivity/specificity, validity and reliability) of delirium scales (diagnostic, measured severity of delirium, or both) available in research and clinical practice.

METHODS

A comprehensive search using the MEDLINE database was conducted to identify the delirium scales in use (1990-2010). The keywords "delirium" and "confusion" were combined with the terms "diagnostic", "questionnaires", "scales", "severity" and "screening" to identify studies that use delirium scales.

This study included scales that were diagnostic, measured severity of delirium, or both. Only original primary validation studies in elderly people were incorporated.

Studies that were not written in English, involved children or used alcohol or drug delirium assessment scales were excluded.

RESULTS

The search strategy yielded 282 potential studies. Only 65 were considered to be of relevance for the purposes of this review. From these, 20 studies met the inclusion criteria for analysis.

Finally 13 studies remained, because 7 studies were excluded (one was not written in English, five involved children and another one used alcohol or drug delirium assessment scales).

Thirteen scales were identified from these thirteen original validation articles. The following seven screening scales were considered: Confusion Assessment Method/CAM [13], Intensive Care Delirium Screening Checklist/ICDSC [14], Delirium Symptom Interview/DSI [15], NEECHAM Confusion Scale/NEECHAM [16], Cognitive Test for Delirium/CTD [17], Delirium Observation Screening Scale/DOSS [18] and Nursing Delirium Screening Scale/Nu-DESC [19].

Six severity scales were also included: Delirium Rating Scale/DRS-98-R [20], Memorial Delirium Assessment Scale/MDAS [21], Confusional State Evaluation/CSE [22], Delirium Severity Scale/DSS [23], Delirium Index/DI [24] and Delirium-O-Meter/DOM [25].

A brief description of each instrument that was separated can be found in the Table **1** and **2**.

These scales were, in this way, compared regarding their main characteristics, in particularly the setting and population, the domain/item description, scoring and administration time as well as their psychometric properties: sensitivity/specificity, validity and reliability. First, the screening scales (Table **1**) were discussed and second the severity instruments (Table **2**).

Most instruments included in this review were based on the DSM-IV [10] and on measure signs and symptoms as described by these criteria.

Two severity rating scales (DI, DOM) were also developed based on the items of screening scales, such as CAM.

The delirium scales diverged in terms of the number of items that are included. The NEECHAM confusion scale was the only test that incorporated physiological parameters.

Most scales were based on a review of selected symptoms of delirium informed by systematic clinical observation, family and/or nurse interviews, medical records and formal brief assessment of mental status (e.g. Mini Mental State Examination – MMSE [26] and Digit Span test – DST [27]).

In these validation studies, the majority of scales were applied by a nurse. However, most of these instruments required appropriate training for their administration.

Regarding administration time, most of these screening and severity scales had a quick performance (e.g. Nu-DESC). In spite of that, additional time is necessary to collect background information, medical charts review and so forth.

The majority of these validation studies occurred in university hospitals, with elderly inpatients from various settings, such medical and surgical wards.

In these studies, the sample size ranged between a minimum of 22 (MDAS) and a maximum of 258 patients (NEECHAM). Only one study (Nu-DESC) reported a priori sample size calculation.

Concerning the psychometric analysis, sensitivity and specificity were evaluated in all screening delirium tests. In the group of severity scales these properties were tested only for DRS-98-R and MDAS.

In the screening scales group, the validity of the results was assessed through their correlations with other delirium scales (DOSS and Nu-DESC studies) and with cognitive screening tests, such as MMSE (CAM, NEECHAM, DOSS studies), as well as with DSM criteria (NEECHAM and Nu-DESC studies).

Considering the severity scales group, in most of the studies (DRS-98-R, MDAS, DI, DOM studies) the validity was assessed by the correlations with the Delirium Rating Scale – DRS [28] and with MMSE (MDAS, DI, DOM studies).

Reliability analysis was assessed in three screening scales studies (CAM, DSI, NEECHAM), using the inter-rater reliability (IRR). The best value of IRR (k=1) was showed by CAM in overall diagnosis.

In the severity scales group, the IRR was calculated with Intra Class Correlation – ICC in two studies (DRS-98-R, DOM). The DRS-98-R showed the highest values in ICC (0.98 to 0.99). Furthermore, in this group, three studies (MDAS, DSS, DI) used the Pearson´s correlation for assess the IRR. The DSS had the highest correlation coefficient (r=0.99).

For the reliability analysis, the majority of these studies assessed the internal consistency - IC, calculating the

Table 1. Characteristics of Delirium Screening/Diagnostic Scales

Scale	Dimensions	Score/Time	Setting/ Population	Sensitivity/ Specificity	Validity	Reliability
CAM [10]	Based on: DSM-III-R, Expert panel 9 delirium features: acute onset, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation and retardation, altered sleep-wake cycle (with 25 items). The first 4 domains are the algorithm for diagnosis.	Diagnosis: presence of the items 1+2 and either 3 or 4 Time: < 5min (without cognitive tests)	Sample 1: General medicine wards (n=30) Sample 2: An outpatient geriatric assessment unit (n=26)	Sens. 100% Spec. 95% (sample1) Sens. 94% Spec. 90% (sample 2)	CAM with: MMSE (k=0.64) Story recall (k=0.59) VAS-AC (k=0.82) Digit Span (k=0.66)	IRR: k=1 (overall diagnosis) k=0.81 (CAM algorithm) (researchers)
ICDSC [11]	Based on: DSM-IV 8 items: altered level of consciousness, inattention, disorientation, hallucinations-delusion-psychosis, psychomotor agitation and retardation, inappropriate speech or mood, sleep/wake cycle disturbance, symptom fluctuation.	Item score: 1=obvious manifestations; 0=no manifestations Total score: range 0 to 8 Time: Not available	ICU of medical and surgical services (n=93)	Sens. 99% Spec. 64% For cut off ≥4		IC: α=0.71 to 0.79
DSI [12]	Based on: DSM-III 7 domains: disorientation, sleep disturbance, perceptual disturbance, psychomotor activity, activity/disturbance of consciousness, general and fluctuating behaviour. 107 items: 63 interview questions, 44 observations items.	Observations items: score 0 to 4 Score are not used as numerical values, and no sum is calculated Diagnosis: presence of disorientation, perceptual and consciousness disturbances Time: Not available	Elderly medical inpatients (n=50)	Sens. 90% Spec. 80%		IRR: k=0.90 (two lay interviewers) k=0.92 (two physicians)
NEECHAM [13]	Based on: research, literature review 9 domains (total 47 items) divided into 3 subscales: Information processing (attention, verbal/motor command of information, memory, orientation); Behaviour (appearance, motor and verbal behaviour); Physiological control (vital functions).	Item score: 0 to 2, 4 or 5 (scale 1 and 2) ; 0 to 2 (scale 3) Total score: range 0 (severe confusion) to 30 (normal) Delirium present ≤24 points Time: <10 min	Two samples of elderly medical inpatients (n=168, n=258)	Sens. 95% Spec. 78% (pilot study, n=168)	Correlations with: DSM-III-R (r= -0.70; r= -0.54) IADL (r=0.47; r=0.64) MMSE (r=0.87) BI (r=0.70) (sample 1) Illness severity (r=0.59) (sample 2)	IC: α=0.90 (sample 1) IC: α=0.90 (sample 2) IRR:k=0.65 (nurse/researcher) (sample 2)
CTD [14]	Based on: DSM-III-R 5 cognitive domains: orientation, attention, memory, comprehension and vigilance.	Each domain: 0-6 (in two-point increments, except for comprehension -single-point) Total score: 0-30 (higher scores = normal) Time: 10-15 min	Post-surgical patients in ICU (n=100)	Sens. 94.7% Spec. 98.8% For cut off <11	All 5 domains scores differentiated: delirium from dementia, schizophrenia and depression (p<0.0001)	IC: α=0.95
DOSS [15]	Based on: DSM-IV 25 items (e.g., Is easy distracted by stimuli from the environment?) Short-version:13 items	Item score: 0 –normal, 1- abnormal behaviour (items: 3, 8, 9 - rated in reverse) Total score: range 0 to 25 Time: 5 min (short-version)	Sample 1: Geriatric medicine inpatients (n=82) Sample 2: Elderly hip fracture inpatients (n=92)	Sens. 94% Spec. 76% (sample 2)	Correlation with: CAM (r=0.63) (sample 1) Correlation with: MMSE (r= -0.66/r=-0.79) IQCDE (r=0.33; r=0.74) BI (r= -0.26; r= -0.55) (sample 1; sample 2)	IC: α= 0.93 (sample 1) α= 0.96 (sample 2)

Table 1. cont...

Scale	Dimensions	Score/Time	Setting/ Population	Sensitivity/ Specificity	Validity	Reliability
Nu-DESC [16]	Based on: DSM-IV 5 items: disorientation, inappropriate behaviour and communication, hallucinations, psychomotor retardation	Item score: 0-1-2 Total score: 0-10 Time: 1 min (mean)	Hemato-oncology and internal medicine units (n=146)	Sens. 98.7% Spec. 86.8% For cut-off >1	Correlation with: DSM-IV (r=0.71) MDAS (r=0.67)	

BI – Barthel Index; **DSM** –The Diagnostic and Statistical Manual of Mental Disorders; **IADL** – Instrumental Activities of Daily Living Questionnaire; **IC** – Internal Consistency; **ICC** – Intra Class Correlation; **ICU** – Intensive Care Unit; **IQCDE** – Informant Questionnaire of Cognitive Decline in Elderly; **IRR** – Inter Rater Reliability; **MMSE** – Mini Mental State Examination; **VAS AC** – Visual Analog Scale for Confusion.

Table 2. Characteristics of Delirium Severity Scales

Scale	Dimensions	Score/Time	Setting/ Population	Sensitivity/ Specificity	Validity	Reliability
DRS-98-R [17]	Based on: DRS 16 items: 13 for severity (sleep-wake cycle, perceptual disturbances, delusions, lability of affect, language, thought process, psychomotor behaviour, orientation, attention, memory, visuospatial ability); 3 for diagnosis (onset/fluctuation of symptoms, physical disorder)	Item score: severity items (0-3), diagnostic items (0 to either 2 or 3) Total score: 0-46 (higher scores = more severity) Time: Not available	Medical, surgical, rehabilitation and nursing home care inpatients (n=68)	Sens. 92% Spec. 93% For cut off ≥15	Correlation with: DRS (r=0.83) CGI (r=0.62) CTD (r= -0.62)	IC:α=0.90 IRR: ICC= 0.98 to 0.99 (psychiatrists)
MDAS [18]	Based on: DSM-IV, ICD-9 10 items: awareness, orientation, short-term memory, digit span, attention, thinking, perception, delusion, psychomotor activity, sleep-wake cycle	Item score: 0-none, 1-mild, 2-moderate, 3-severe Total score: 0-30 Time:10 min	Inpatients with advanced degree of cancer (n=22, n=51)	Sens. 71% Spec. 94% For cut off of 12/13	Correlation with: MMSE (r= -0.91) DRS (r=0.88) CGRSS (r=0.89) MDAS differed delirium from other cognitive impairment disorder (p<0.0002)	IC: α=0.91 IRR: r=0.92 (two psychiatrists)
CSE [19]	Based on: Literature, clinical experience 22 items: 12 of which measure "key symptoms": disorientation, thought and memory disturbances, inability to concentrate, distractibility, perseveration, impaired contact, paranoid delusions and hallucinations	Total score: sum of 12 items, with a maximum of 30 points Time: Not available	Nursing home, Orthopaedic and Psychogeriatric units (n=71)		CSE against global-rating by psychiatrists (r=0.79)	IRR: k=0.38–0.93 (researchers)
DSS [20]	Based on: WAIS-R Included of tests: forward digit span - FDS, cognitive similarities - CS	Total score: max. 24 (FDS) and max. 35 (CS) Time: 10 min	Elderly medical inpatients (n=37)		Correlation with expert ratings (r=0.49, 0.43)	IRR: r=0.99 (researchers)
DI [21]	Based on: DSM-III-R, CAM 7 items: inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation/retardation	Item score: 0-absent, 1 -mild, 2 – moderate, 3-severe Total score: 0-21 Time: Not available	Medical inpatients, with delirium diagnoses, according CAM (n=30, n=37)		Correlation with: DRS (rs= 0.84) (sample 1) MMSE (r= -0.70) BI (r= -0.60) IQCDE* (r= -0.26) IADL* (r= -0.42) *Status prior to admission (sample 2)	IRR: r=0.78 (researchers) r= 0.88 (researchers,psychiatrists) (sample 1)

Table 2. cont...

Scale	Dimensions	Score/Time	Setting/ Population	Sensitivity/ Specificity	Validity	Reliability
DOM [22]	Based on: DSM-IV, CAM, NEECHAM, DOSS 12 items: sustained and shifting of attention, orientation, consciousness disturbance, apathy, psychomotor retardation, incoherence, fluctuating functioning (diurnal variation/sleep-wake cycle), restlessness (psychomotor agitation), delusions, hallucinations, anxiety/fear	Item score: 0=absent, 1=mild disturbances 2=moderate, 3=severe Total score: 0-36 Time: 3-5 min	Geriatric Care Unit Inpatients (n=92)		Correlation with: DOSS (r_s=0.89) DRS-98-R (r_s=0.87) MMSE (r_s= -0.83) GIP28 (r_s=0.92 to 0.56) DOM differentiated delirium from non delirium patients ($p<0.001$)	IC:α=0.87 to 0.92 IRR: ICC=0.84-0.91 (nurses)

BI – Barthel Index; **CGI** – Clinical Global Impression; **CGRSS** – Clinician's Global Rating of Delirium Scale; **DOSS** – Delirium Scale Observation; **CTD** – Cognitive Test for Delirium; **DRS** –Delirium Rating Scale; **DSM** –The Diagnostic and Statistical Manual of Mental Disorders; **IADL** – Instrumental Activities of Daily Living Questionnaire; **IC** – Internal Consistency; **ICC** – Intra Class Correlation; **ICD9** – International Statistical Classification of Diseases; **IQCDE** – Informant Questionnaire of Cognitive Decline in Elderly; **IRR** – Inter Rater Reliability; **MMSE** – Mini Mental State Examination; **WAIS-R** –The Wechsler Adult Intelligence Scale - Revised.

Cronbach's alpha coefficient (α). This coefficient was high in the DOSS (α=0.96) and in the DOM (α= 0.92) in severity scales.

DISCUSSION

Thirteen scales for the early evaluation of delirium have been retrieved. Some of them are more likely to be used while others present limits based beyond their psychometric properties, other relevant factors. There are some aspects that have to be present, such as the purpose of the scale (for diagnosis or for measuring symptom severity), the nature of data on which the rating is based (e.g. brief cognitive tests vs. interview), the setting used (surgical vs. cancer units), the number of items, administration procedures, response format, scoring, amount of time available and rater training required [29].

Beyond this, it is also important to ensure that the symptoms surveyed are consistent with the symptoms of delirium as specified in DSM IV criteria [7]. The diagnosis based on key features will help to distinguish delirium from other neuropsychiatric disorders (e.g. dementia).

The majority of the instruments included in the present study were developed by operationalizing the DSM criteria. However, most of them do not include some important features (e.g. ICDSC, DOM), such as sudden onset or fluctuation course. In this way, CAM (long version) and DRS-98-R fulfill the entire DSM definition most completely, providing a comprehensive and detailed evaluation of the most pertinent clinical features. Besides, the use of this CAM version is recommended to maximize sensitivity for detection in delirium [30, 31].

On the other hand, CAM is based not only on the observations during the interview (as are most of the screening scales included in this study), but also on information from the family members and/or medical and nursing staff, as well as results from formal cognitive tests.

The collection of collateral information becomes crucial due to the fluctuating course and incertitude of answers of older people not able to provide accurate information [7]. Besides, the delirium scales are intended to be used in conjunction with standardized cognitive tests. This neuropsychological assessment should include measurement of attention, because an alteration in this domain is one of the hallmarks of delirium [32].

Considering the severity scales group, DRS-98-R is the only instrument where all these sources of available information are applicable.

Most of the scales were developed by and for nurses (e.g. NEECHAM, NU-DESC) or to be used by psychiatrists (DRS-98-R, MDAS). The CAM was designed specifically to allow a non-psychiatric clinician, to diagnose delirium quickly and accurately. However, some training is recommended for optimal use [31], especially when considering it as screening instrument [33, 34].

In spite of the fact that DRS-98-R has been developed for psychiatrists' use, other clinicians can also use it, but only after training [20].

In this context, a manual with instructions for administration and scoring could improve the performance of these scales. CAM and DSI are the only scales which have one, but the first one has a more comprehensive manual, with general and specific instructions, for each item. Besides that, it includes recommended training procedures, as well as a test to assess knowledge about delirium and CAM scoring. Related to the severity scales, only DRS-98-R incorporated general information and specific instructions for each domain assessed.

The structure of these scales varies between the tests, in terms of response format, number and scoring of items, but it is important to note that CAM and DSI as screening scales, and DRS-98-R and MDAS as severity measures, can have advantages in this point. They include exact instructions on how to present each question, specific tasks, examples of behaviours and how to score each item. Whereas DSI is very lengthy (with 107 items, which limit its application in routine care), CAM can be completed in less than 5 minutes (without cognitive tests application) [13].

This scale also provides a simple diagnostic algorithm, which includes the cardinal features of DSM criteria [13].

Another important point, despite the good psychometric properties in their primary study, is the lack of further validation studies for the remaining scales (e.g. DSI, Nu-DESC, DSS and DOM) [29].

On the other hand, CAM and DRS-98-R have been the most widely used as standardized delirium instruments for both clinical (mainly with elderly inpatients) and research purposes. Both have been translated into many languages and used in several studies [30, 31, 32]. The CAM has also been adapted for other specific clinical settings, such as intensive care units, emergency departments and nursing homes [31].

Comparing the psychometric characteristics, CAM and DRS-98-R revealed good psychometric properties, in particular high sensitivity/specificity and good inter-rater reliability. The reliability of delirium rating scales is important, due to their potential clinical usefulness, with implications for the ability of clinicians to discriminate from other causes of cognitive impairment in practice [35, 36].

Recent review studies [12, 29, 37, 38, 39] corroborated this preference for CAM (for diagnosis) and for DRS-98-R (for severity). However, some of these studies [38, 39] concluded that CAM and the NEECHAM and DOSS, appear to be the most suitable screening and diagnostic instruments for delirium, depending on the type of (trained) rater being a physician or nurse.

The international guidelines [7, 40] suggest screening for cognitive impairment on hospital admission of elderly patients, using a brief cognitive test (e.g. MMSE), followed by the CAM in order to detect delirium and the DRS-98-R for measuring the severity of delirium states.

In spite of this, the most recent guidelines [3] recommended first of all that it is essential to identify the elderly patients hospitalized or in a long-term care unit, with risk factors of developing delirium. If any of these patients present recent (within hours or days) changes or fluctuations in cognitive function, perception, physical function and social behavior, a clinical assessment should be carried out, based on the DSM-IV criteria or short CAM (algorithm) to confirm the diagnosis. This evaluation should also be carried out by a trained healthcare professional.

In the present review, we have only reported the primary development studies of delirium assessment scales included. No further studies replicating the scale´s results have been integrated into this review. Moreover, articles where the psychometric properties of two or more different scales are compared have not considered.

Another potential limitation of this review process is based on the fact we conducted a qualitative data synthesis, by summarizing, comparing and contrasting primary article results. No standard techniques or criteria were used for a quantitative analysis of validity assessment of these studies.

Besides, this review may be also limited by the inclusion of articles published only in English.

The present work appears as a contribution to an up-to-date overview of delirium assessment in a clinical psychiatric context. However, the results of this review should be interpreted bearing in mind the approach included in these studies.

CONCLUSION

Despite the relevance of delirium, it is frequently under-recognized in clinical practice. The use of protocols to identify patients at high risk of delirium, systematic assessment of mental status in older inpatients by healthcare professionals with previous training, as well as the use of screening delirium scales may improve early detection, diagnosis and appropriate management of this condition. Despite the many scales available, there is evidence to support the use of CAM as a diagnostic instrument and the DRS-98-R as a measure of delirium symptom severity in effective assessment.

In the elderly delirium assessment tools field, the comparability of psychometric properties reported in validation studies has to be improved. Future development and refinement of these instruments will be required. However, there are some important issues that need to be considered in further validation research, such as appropriate sample selection size (mainly for appropriate use of reliability statistics), correct use of reference standards and assessment of the clinical impact of the instruments, as well as correlations with delirium outcomes.

Finally, an educational intervention has to be implemented in order to improve the ability of different healthcare professionals to identify delirium with more accuracy and validity.

CONFLICT OF INTEREST

No conflict of interest.

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7 O IMPACTO DO DELIRIUM NA FAMÍLIA/CUIDADORES

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RESUMO

Contexto: O delirium surge como experiência bastante traumática, não só para os doentes, mas também para os familiares e/ou cuidadores. Objectivo: Analisar e sintetizar os estudos existentes sobre o nível de stress provocado pelo delirium nos familiares e/ou cuidadores. Metodologia: Revisão não sistemática da literatura, de artigos publicados na PubMed (2000 a 2012), cruzando o termo "delirium" com "distress", "impact" e "family", "caregiver", "relatives". Foram considerados como critérios de inclusão: diagnóstico de delirium padronizado e/ou instrumento de avaliação e ponderação do nível de stress de uma forma sistemática em familiares de doentes adultos/idosos com delirium. Os estudos em língua não inglesa e de casos clínicos foram excluídos. Resultados: De trinta e oito artigos identificados inicialmente, foram considerados onze para análise. De um modo geral, as famílias (sobretudo os mais jovens e do sexo masculino) revelaram níveis de stress bastante elevados e mesmo superiores aos registados para os profissionais de saúde e para os doentes, estando associados a diversos factores, como agravamento do estado de saúde do doente e presença de agitação psicomotora. Além disso, a família interpretava esta experiência como um sinal de aproximação da morte, resultado de dor/desconforto ou dos efeitos de medicação. Verificou-se ainda uma relação entre o delirium e a presença de ansiedade generalizada nestes familiares. Conclusões: As repercussões negativas associadas ao delirium, apontam para a necessidade de desenvolvimento de intervenções de suporte dos familiares, bem como a avaliação da sua eficácia, nomeadamente quanto aos elevados níveis de stress identificados.

PALAVRAS-CHAVE: **delirium; família; cuidador; stress psicológico**

RESUMEN

Introducción: El delirium surge como una experiencia muy traumática, no sólo para los pacientes sino también para los miembros de la familia/cuidadores. Objetivo: Analizar y sintetizar los estudios existentes sobre los niveles de estrés causados por el delirium en la familia/cuidadores.

Metodología: Revisión no sistemática de la literatura, de artículos publicados en PubMed (2000-2012), que cruza el término "delirium" con "distress", "impact" y "family", "caregiver", "relatives". Se consideraron como criterios de inclusión: diagnóstico de delirium estandarizado y/o instrumentos de evaluación, y ponderación del nivel de estrés de forma sistemática en los familiares de los pacientes adultos/ancianos con delirium. Se excluyeron los estudios en lengua no-inglesa y los casos clínicos.

Resultados: De treinta y ocho artículos identificados inicialmente, se consideraron once para los análisis. En general, las familias (especialmente los más jóvenes y hombres) revelaron altos niveles de estrés e incluso superiores a los registrados para los profesionales sanitarios y los pacientes, y se asocian con varios factores tales como el empeoramiento del estado de salud del paciente y la presencia de agitación psicomotora. Además, la familia interpretaba esta experiencia como una señal de muerte inminente, como resultado de dolor/incomodidad o efectos de la medicación. Se observó aún una relación entre el delirium y la presencia de ansiedad generalizada en estas familias. Conclusiones: Los impactos negativos asociados con el delirium apuntan para la necesidad de desarrollar intervenciones para apoyar a la familia, así como la evaluación de su eficacia, sobre todo con respecto a los altos niveles de estrés identificados.

DESCRIPTORES: **delirium; família; cuidador; estrés psicológico**

ABSTRACT

Background: Delirium appears as a psychologically traumatic experience, not only for patients, but also for their family or caregivers Aim: To analyze and synthesize existing studies about the level of distress caused by delirium in the family and/or caregivers. Methods: Non-systematic review of literature, of published articles in PubMed (2000-2012), using the term "delirium" with "distress", "impact" and "family", "carer", "relatives". The following were considered as inclusion criteria: diagnosis of delirium with standardized criteria and/or assessment instruments, and assessment of the level of distress in a systematic way in families of adults/elderly patients with delirium. Studies not carried out in English, and clinical cases were excluded. Results: From thirty-eight articles initially identified, eleven were considered for analysis. Generally, family members (above all the youngest and those who were male) showed quite high levels of psychological distress even higher than reported by health professionals and by patients, as they were linked to several factors, such as worsening of medical condition of the patient and the presence of psychomotor agitation. In addition, family members interpreted this experience as a sign of approaching death, result of pain/discomfort or medication effects. There was also a relationship between delirium and the presence of generalized anxiety in these families. Conclusion: The negative consequences associated with delirium, point to the need for the development of support interventions for family members, as well as the assessment of their efficacy, particularly in the high levels of distress identified.

KEYWORDS: **delirium; family; caregiver; psychological stress**

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INTRODUÇÃO

Com o aumento da população idosa em todo o mundo, as perturbações neuropsiquiátricas como o delirium (ou estado confusional agudo) adquirem inevitavelmente maior importância, afectando mais de 30% dos idosos hospitalizados (Saxena & Lawley, 2009).

O delirium caracteriza-se por alterações do nível da consciência, da cognição ou da percepção (não atribuídas a demência preexistente ou estabelecida), que se desenvolve ao longo de um curto período de tempo (horas/dias), com curso flutuante. Acresce ainda, pela história clínica e exames físicos/laboratoriais, o facto de ser uma perturbação causada por doença médica, intoxicação/abstinência de substância ou por múltiplas etiologias (American Psychiatric Association[APA], 2000). Esta síndrome neuropsiquiátrica surge como um problema grave, potencialmente evitável e, muitas vezes, não reconhecido, estando por isso relacionado com o aumento da morbilidade e da mortalidade nestes doentes (Siddiqi, House, & Holmes, 2006).

De modo consistente com estes dados, torna-se fundamental uma identificação precoce e uma intervenção adequada que contribuam para a diminuição das consequências associadas a esta perturbação (National Institute for Health and Care Excellence[NICE], 2010). Neste contexto, o envolvimento das famílias e/ou dos cuidadores no reconhecimento do delirium, bem como na prestação de cuidados ao doente, desempenham um papel crucial (O'Malley, Leonard, Meagher, & O'Keeffe, 2008). As informações dos familiares e/ou cuidadores sobre o estado cognitivo prévio do doente, bem como sobre alterações do estado mental observadas durante o internamento hospitalar, quando partilhadas com os profissionais de saúde, podem ser úteis para a avaliação de algumas das características do delirium, nomeadamente o seu início agudo e o curso flutuante e, poderão igualmente auxiliar no diagnóstico diferencial com demência (Martins e Fernandes, 2012).

A inclusão da família na abordagem do delirium assenta ainda na importância da sua presença junto do doente e na ajuda prestada no processo de comunicação e na sua reorientação. O delirium tem sido descrito como uma experiência bastante desagradável pelos doentes, sobretudo pelas emoções vivenciadas durante este episódio, nomeadamente medo, ansiedade e sensação de ameaça. Em muitos casos, estas surgem associadas à presença de perturbação da percepção e de delírios (O'Malley et al., 2008), podendo a presença da família ajudar o doente a lidar de forma mais ajustada. Neste âmbito, alguns estudos (ex. Stenwall, Sandberg, Eriksdotter Jonhagen, & Fagerberg, 2008) referem que os doentes consideraram ter sido benéfico e reconfortante a presença dos seus familiares durante o episódio de delirium, valorizando a sua intervenção de suporte.

Por outro lado, a família poderá ainda ajudar os profissionais de saúde na comunicação eficaz com o doente, bem como na sua reorientação, através do uso de diversas estratégias (ex. repetição da data, hora, local, motivo pelo qual está internado, ou identificação das pessoas presentes). A disponibilização de objectos familiares (ex. fotografias, calendário e relógio), bem como de ajudas instrumentais (ex. óculos, aparelho auditivo) facilita também este processo de reorientação (Caraceni & Grassi, 2011).

Contudo, e apesar da integração da família na abordagem do delirium ter sobretudo consequências benéficas, há que ter em consideração que poderá tornar-se numa experiência traumática, para além dos doentes, também para os seus familiares, que revelam níveis elevados de stress perante estas situações (ex. Breitbart, Gibson, & Tremblay, 2002; Bruera et al., 2009).

O presente artigo pretende analisar e sintetizar os estudos existentes sobre o nível de stress provocado pelo delirium nos familiares e/ou cuidadores.

METODOLOGIA

Este estudo consiste numa revisão não sistemática da literatura, de artigos publicados na PubMed, no período de 2000 a 2012, cruzando o termo "delirium" com "distress", "impact" e "family", "caregiver", "relatives". Foram considerados os seguintes critérios de inclusão: (1) diagnóstico de delirium com critérios padronizados (ex. Diagnostic and Statistical Manual of Mental Disorders/DSM-IV-TR) (APA, 2000) e/ou instrumento de avaliação e (2) avaliação do nível de stress de uma forma sistemática em familiares de doentes adultos/idosos com delirium. Os estudos em língua não inglesa, bem como os casos clínicos, foram excluídos desta revisão.

Na pesquisa inicial, os resumos identificados foram avaliados por dois autores desta revisão, de forma independente e cega, obedecendo rigorosamente aos critérios de inclusão e exclusão previamente definidos. Caso não fossem suficientemente esclarecedores, procedeu-se à análise do artigo na íntegra. Posteriormente, possíveis discordâncias foram resolvidas por consenso entre autores. Os estudos que cumpriram os critérios de inclusão foram avaliados e comparados quanto às seguintes características: objectivo, desenho de estudo, amostra, contexto, critérios de inclusão e exclusão, instrumentos de avaliação do nível de stress e principais resultados. Foi igualmente efectuada uma análise da bibliografia dos artigos seleccionados.

RESULTADOS

Num primeiro momento, foram identificados trinta e oito artigos, dos quais onze foram recrutados para análise. Destes, foram excluídos três. Da análise à bibliografia dos artigos seleccionados, foram ainda adicionados mais três artigos, perfazendo um total de onze estudos (cinco transversais, um prospectivo, três qualitativos e duas revisões da literatura). Os principais dados relativos aos níveis de stress na família/cuidadores extraídos dos estudos analisados estão sumarizados na Tabela 1.

TABELA 1 - Principais resultados dos estudos analisados

ESTUDO	TIPO DE ESTUDO	AMOSTRA	AVALIAÇÃO	PRINCIPAIS RESULTADOS
Breitbart, Gibson, & Tremblay, 2002	Prospectivo	76 familiares de doentes internados por cancro	Delirium Experience Questionnaire – Questão: "Qual o seu nível de stress durante o episódio de delirium no seu familiar doente?" Cotada de 0 – (nenhum) a 4 (muito stressante).	76% dos familiares demonstraram níveis elevados de stress, sobretudo associados ao agravamento do estado de saúde do doente, significativamente superiores aos encontrados para os enfermeiros e doentes.
Morita, Hirai, Sakaguchi, Tsuneto, & Shima, 2004	Transversal	195 familiares de doentes com cancro terminal (delirium antes da morte)	Desenvolvimento de questionário de avaliação da identificação e frequência de 12 sintomas de delirium. Avaliação do nível stress para cada sintoma identificado, numa escala de 0 (nenhum) a 4 (muito stressante).	Mais de 2/3 dos familiares identificaram todos os sintomas (excepto sonolência), como sendo geradores de stress, quando ocorriam frequentemente ou muito frequentemente
Buss et al., 2007	Transversal	200 cuidadores de doentes com cancro (esperança média de vida inferior a seis meses)	Questão: "No último mês, quantas vezes observaram o doente confuso?" (0 - nunca a 4 – todos os dias). Entrevista Clínica Estruturada para o DSM-IV (SCID) - Eixo I, para diagnóstico de perturbação psiquiátricas.	Cuidadores que observaram episódio de delirium apresentaram doze vezes mais probabilidade de sofrerem de perturbação de ansiedade generalizada, comparando com os que não tinham assistido.
Namba et al., 2007	Qualitativo	20 familiares de doentes com cancro terminal (delirium duas semanas antes da morte)	Entrevista semi-estruturada, com foco na percepção do delirium e emoções associadas. Nível de stress avaliado com base na análise de conteúdo.	70% dos familiares apresentaram níveis de stress, relacionados com: culpa, ansiedade e preocupação, desamparo e exaustão. Interpretaram esta experiência como sinal de aproximação da morte, ansiedade relacionada com a morte, resultado de dor ou de efeitos de medicação.
Morita et al., 2007	Transversal	242 familiares de doentes com cancro (delirium duas semanas antes da morte)	Desenvolvimento de questionário de avaliação para identificação de sintomas de delirium. Avaliação do nível de stress, através da questão: "Qual o seu nível de stress durante o episódio de delirium no seu familiar doente?" Cotada de 1 (nenhum) a 5 (muito stressante). Escalas de tipo Likert para avaliação de emoções e potenciais causas do delirium.	32% dos familiares revelaram elevados níveis de stress (a agitação foi o factor determinante). Mais de 50% reportou as seguintes emoções: ambivalência, culpabilidade e preocupação em estar com o doente. Interpretaram esta experiência como: – sinal de aproximação da morte, parte do processo de morte, sonho, fenómeno transcendente, alívio do sofrimento actual, resultado de dor e desconforto e efeitos de medicação
Stenwall, Sandberg, Eriksdotter Jonhagen, & Fagerberg, 2008	Qualitativo	10 familiares de doentes internados em hospitais	Entrevista semi-estruturada (análise de conteúdo).	Os familiares apresentaram sentimentos de perda, desconfiança e insegurança, ao observarem o episódio de delirium no familiar doente.
Bruera et al., 2009	Transversal	99 familiares cuidadores de doentes com cancro	Lista de sete sintomas de delirium: avaliação da frequência (escala de 0 - ausente a 4 - maior parte do tempo) e o nível de stress associado (escala de 0- nenhum a 4 - extremamente stressante).	Familiares revelaram elevados níveis de stress, para a maioria dos sintomas observados, superiores aos dos doentes.
Cohen, Pace, Kaur, & Bruera, 2009	Qualitativo	37 cuidadores familiares de doentes com cancro avançado	Entrevista fenomenológica (análise de conteúdo).	Descrevem esta experiência como stressante, terrível, frustrante e assustadora. Atribuem o delirium à medicação para a dor.
Bull, 2010	Transversal	30 familiares de doentes de centros de dia	Desenvolvimento do Family Caregiver Distress Questionanire, com avaliação do nível de stress numa escala de 0 (nenhum) a 10 (muito stressante) face a cada sintoma identificado numa escala de avaliação de delirium	Apenas 9 familiares reportaram quatro a seis sintomas de delirium, revelando níveis baixos de stress. (média: 16.55/escala 0-60).
O'Malley, Leonard, Meagher, & O'Keeffe, 2008	Revisão da literatura	Artigos sobre experiência de delirium no doente, família e profissionais de saúde	Análise dos resultados de 4 estudos sobre o impacto do delirium na família	Os familiares assumem um papel fundamental no tratamento e no cuidar do doente com delirium. Reporta a necessidade de reconhecer e minimizar as necessidades dos cuidadores e o nível de stress provocado por esta perturbação.
Partridge, Martin, Harari, & Dhesi, 2012	Revisão da literatura	Artigos sobre a capacidade de recordar a experiência do delirium pelo doente e o seu impacto no doente, família e profissionais de saúde	Análise dos resultados de 9 estudos sobre o impacto do delirium na família	Os familiares demonstram níveis de stress elevados, podendo ser superiores ao dos doentes. São necessários mais estudos sobre: – Associação entre nível de stress e morbilidade psicológica. – Papel da informação/educação na redução do stress.

A maioria dos estudos integrou amostras de familiares (na sua maioria adultos, do sexo feminino e cônjuges) de doentes idosos, internados em cuidados paliativos, com recurso a metodologias quantitativas e escalas de tipo Likert, para a avaliação do nível de stress provocado por delirium. Alguns estudos avaliaram estes níveis face ao delirium na sua globalidade (ex. Breitbart et al., 2002) enquanto que outros avaliaram face a cada um dos sintomas percepcionados pelos familiares (ex. Bruera et al., 2009).

De um modo geral, as famílias e/ou cuidadores revelaram níveis de stress bastante elevados e mesmo superiores aos registados para os profissionais de saúde e para os doentes (Breitbart et al., 2002; Bruera et al, 2009), sendo sobretudo associados ao agravamento do estado de saúde do doente, presença de agitação psicomotora, sintomas psicóticos, labilidade emocional e discurso incoerente (Breitbart et al., 2002; Morita, Hirai, Sakaguchi, Tsuneto, & Shima, 2004; Morita et al., 2007).

Importa igualmente referir que, não só é elevado o número de familiares que consideram o delirium como uma experiência extremamente stressante, mas também o grau deste nível de stress é considerado como grave e/ou substancial (Breitbart et al., 2002; Bruera et al., 2009).

Além disso, a família interpretava esta experiência como um sinal de aproximação da morte, resultado de dor/desconforto ou dos efeitos de medicação (Cohen, Pace, Kaur, & Bruera, 2009; Morita et al., 2007; Namba et al., 2007), o que contribuiu, igualmente, para os elevados níveis de stress apresentados.

Morita et al (2007) verificaram ainda que estes níveis mais elevados de stress foram sobretudo reportados pelos familiares mais jovens e do sexo masculino.

Finalmente, Buss et al (2007) constataram a presença de uma associação significativa entre delirium e ansiedade generalizada, que se manteve após controlo de variáveis como a sobrecarga do cuidador e outras experiências stressantes relacionadas com o doente.

DISCUSSÃO

Apesar da elevada morbilidade e mortalidade associadas ao delirium estar bem documentada, existem poucos estudos sobre as suas repercussões nos familiares e/ou cuidadores destes doentes (O'Malley et al., 2008; Partridge, Martin, Harari, & Dhesi, 2012).

À escassez dos trabalhos que estudam estas consequências na família, associa-se a difícil comparação dos respectivos resultados pela utilização de diferentes métodos de avaliação dos níveis de stress (avaliação global do delirium vs. avaliação face a cada sintoma), inclusão de diferentes grupos/amostras de estudo (delirium terminal vs. delirium reversível) e diversificação de contextos (cuidados paliativos vs. enfermarias).

Para além desta heterogeneidade dos estudos, deve ser salientado que a maioria dos estudos selecionados integrou familiares de doentes com cancro em fase terminal, pelo que é necessário esclarecer se os elevados níveis de stress identificados correspondem ao delirium propriamente dito, ou são explicados por outras variáveis como a percepção da aproximação da morte (Bruera et al., 2009, Partridge et al., 2012).

Por outro lado, deve igualmente destacar-se a variabilidade das interpretações dadas pelos familiares aos sintomas de delirium (Morita et al., 2004). Ainda assim, e apesar dos limites assinalados, é possível constatar que a ocorrência de um episódio de delirium causa um impacto significativo e negativo nestes familiares, traduzido em níveis aumentados de stress.

Um outro dado relevante prende-se com o facto dos familiares identificarem um maior número de sintomas no doente durante o episódio, em comparação com os profissionais de saúde, sugerindo que os familiares podem constituir uma fonte fidedigna de informação e/ou observação do comportamento do doente durante o seu internamento, bem como da sua resposta ao tratamento em curso. No entanto, esta identificação de sintomas pelos familiares poderá ser sobrevalorizada pela ansiedade associada à situação vivenciada (Bruera et al., 2009) e que deve ser igualmente salvaguardada.

Por outro lado, a discrepância na identificação de sintomas por familiares e profissionais, poderá contribuir para que o delirium constitua, frequentemente, um factor de conflito, na medida em que surgem diferentes perspectivas quanto ao sofrimento do doente e à necessidade de intervenção (Bruera et al., 2009).

Salvaguardando o eventual efeito subjectivo associado à carga emocional da situação vivenciada pelos familiares, tem sido recomendado que as observações quanto aos sintomas/comportamentos do doente devem ser consideradas, com recurso a escalas de observação ou a instrumentos de avaliação estandardizados (Bruera et al., 2009), reduzindo o risco de viés. Neste plano, destaca-se o Family Confusion Assessment Method/FAM-CAM (Steis et al., 2012) desenvolvido recentemente como um método de detecção do delirium, de fácil aplicação e cotação, sendo preenchido com base nas informações/observações de familiares e/ou cuidadores.

Finalmente, as repercussões negativas associadas ao delirium e descritas nos estudos analisados, apontam para a necessidade de intervenções psicoterapêuticas e/ou psicoeducativas de suporte ao familiar, com o objectivo de o ajudar ao longo de todo este processo (Caraceni & Grassi, 2011; NICE, 2010). A necessidade de mais estudos sobre a experiência do delirium, bem como sobre o impacto destas intervenções, nomeadamente na redução da ocorrência, gravidade e duração desta perturbação, foi destacada pelas mais recentes guidelines (NICE, 2010).

De um modo geral, estas intervenções devem considerar os seguintes princípios: a) identificar e responder às preocupações e necessidades dos familiares; b) identificar as reacções emocionais, que possam ter como consequência comportamentos desadequados (ex. redução do número de visitas ao doente); c) promover a comunicação entre a família e os profissionais de saúde responsáveis pelo doente; d) envolver a família no plano de cuidados/assistência; e) disponibilizar informação/educação sobre o delirium (Caraceni & Grassi, 2011).

No que concerne a este último ponto, a componente educativa deve focalizar-se na abordagem dos seguintes aspectos do delirium: sintomas (em particular desinibição, agitação, alucinação e delírios); curso flutuante (as fases transitórias em que o doente parece estar bem não significam, necessariamente recuperação); possíveis causas (ex. alterações metabólicas, medicação, relação com demência) e opções de tratamento (incluindo efeitos secundários dos tratamentos farmacológicos) (Caraceni & Grassi, 2011; NICE, 2010).

Neste âmbito, os familiares que participaram nos estudos de Gagnon et al (2002) e de Keyser, Buchanan, e Edge (2012), com intervenções psicoeducativas, consideraram fundamental a disponibilização de informação sobre o delirium (ex. factores de risco, sinais de delirium) a todos os familiares e/ou cuidadores.

A presente revisão surge como um contributo para uma melhor compreensão do estado da arte sobre a experiência do delirium vivenciada pelos familiares e/ou cuidadores.

O processo de revisão baseou-se numa análise qualitativa, sintetizando os principais resultados dos artigos incluídos, não recorrendo a qualquer técnica ou critério estandardizado. Além disso, salienta-se que os resultados apresentados devem ser analisados, tendo em consideração as limitações já referidas, dos estudos incluídos no presente trabalho.

CONCLUSÕES

É actualmente reconhecida a importância do papel que as famílias e/ou cuidadores desempenham no reconhecimento e na prestação de cuidados ao doente com delirium. Esta consciencialização é paralela à identificação dos elevados níveis de stress e dificuldades emocionais envolvidas, que podem comprometer a assistência prestada ao doente e, nessa medida, devem também ser identificados e alvo de intervenção.

Neste sentido, torna-se indispensável o desenvolvimento de intervenções de suporte, com a avaliação da sua eficácia, nomeadamente na redução destes níveis de stress vivenciados por estes familiares e/ou cuidadores.

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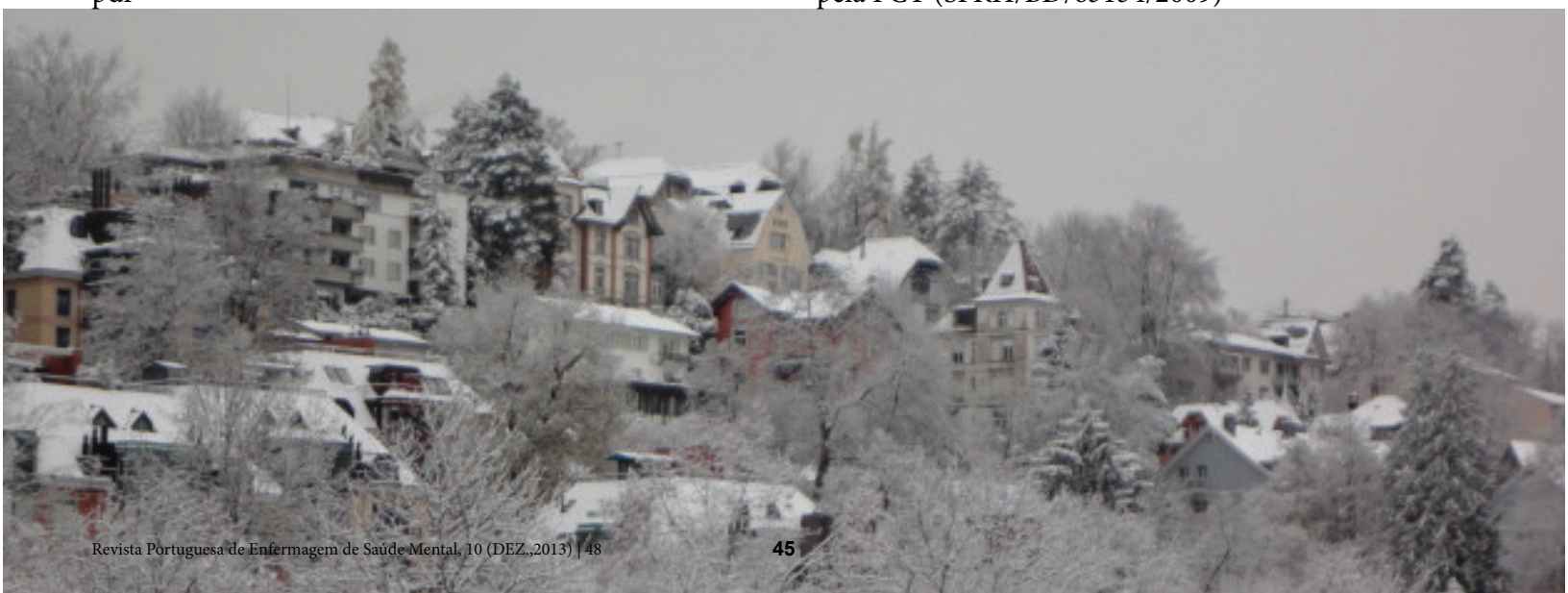

3. INVESTIGAÇÃO EMPÍRICA

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Rapid Communication

Pilot study on the European Portuguese version of the Confusion Assessment Method

Martins S, Moldes P, Pinto-de-Sousa J, Conceição F, Paiva JA, Simões MR, Fernandes L. Pilot study on the European Portuguese version of the Confusion Assessment Method

Objective: To present the pilot study on the European Portuguese validation of the Confusion Assessment Method (CAM).
Methods: The translation process was carried out according to International Society Pharmacoeconomics and Outcomes Research guidelines with trained researchers and inter-rater reliability assessment. The study included 50 elderly patients, admitted (≥24 h) to two intermediate care units. Exclusion criteria were: Glasgow Coma Scale (total score ≤11), blindness/deafness, inability to communicate and not able to speak Portuguese. The sensitivity and specificity of CAM were assessed, with DSM-IV-TR criteria of delirium used as a reference standard.
Results: Findings revealed excellent inter-rater reliability ($k > 0.81$), moderate sensitivity (73%) and excellent specificity (95%).
Conclusion: These preliminary results suggested that this version emerges as a promising diagnostic instrument for delirium.

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Keywords: aged; CAM; delirium; Portugal; validation studies

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Significant outcomes

- The European Portuguese version of the Confusion Assessment Method showed good feasibility, very good inter-rater reliability, moderate sensitivity and excellent specificity, which suggested that it emerges as a promising tool in the diagnosis of delirium in the elderly.

Limitations

- It was carried out only in an intermediate care unit and there was a long interval (1–7 h) between the two assessments.

Introduction

Delirium is a serious and common neuropsychiatric syndrome in elderly hospitalised patients (1). It has been associated with negative clinical outcomes that have been well documented, such as the increase of mortality, length of hospital stay and institutionalization (2). In view of the above, its early detection is very important to reduce morbidity and mortality in these patients. The use of standardised instruments in routine clinical practice can help in recognising symptoms, rating clinical improvement evaluating the effectiveness of interventions (3).

In this context, the Confusion Assessment Method (CAM) (4) is a widely used and highly accurate delirium-screening instrument, based on the DSM-III-R criteria (5), for use by trained health professionals.

The CAM assesses the presence, severity and fluctuation of nine delirium features (long version): acute onset and fluctuating course*, inattention*, disorganised thinking*, altered level of consciousness*, disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation, and altered sleep–wake cycle. This instrument also includes a diagnostic algorithm (short version), based on the four cardinal features of delirium (previously marked with an asterisk). Delirium diagnosis requires the presence of features 1 and 2, and either 3 or 4.

In the original study (4), CAM demonstrated sensitivity of 94–100%, specificity 90–95%, when validated against the ratings of geriatric psychiatrists, and high inter-rater reliability ($k = 0.81–1.0$). More recently, in a systematic review (6) of seven high-quality studies ($n = 1071$) evaluating the performance of the CAM, combined sensitivity was 94% [95% confidence interval (CI) = 91–97%], and specificity was 89% (95% CI = 85–94%). The CAM has been translated and validated into various languages (7), as well as recommended by the most recent guidelines (8).

The aims of this study were to present the European Portuguese translation and cultural adaptation process and the pilot study of CAM (long version).

Materials and methods

Translation and adaptation process

This process was carried out according to the guidelines suggested by The Translation and Cultural Adaptation Group of the International Society Pharmacoeconomics and Outcomes Research (9), as follows:

- Preparation: permission to use the CAM from the author.
- Forward translation of the original instrument into the target language independently by two translators, health professionals.
- Reconciliation of the two forward translations into a single translation.
- Back translation into English by an independent professional, without any information about the original or other versions.
- Back translation review/harmonisation: the various versions were compared with detect any translation discrepancies and to ensure conceptual equivalence between versions.
- Cognitive debriefing
  - Eight health professionals (psychiatrists, psychologists and nurses) read and examined the translated version to assess the level of comprehensibility, the cognitive equivalence and to detect any unclear words, concepts or other elements that they were unable to understand.
  - One of the authors (L.F.) who is a geriatric psychiatry specialist, with clinical and research expertise regarding delirium, trained the researchers, a psychologist (S.M.) and a psychiatry resident (P.M.), based on the original training manual (10). This included: four training sessions of 2 h (clinical overview about delirium, general overview on the cognitive assessment instruments, and the CAM and fulfilment of CAM pretest), one-on-one session (the researchers practiced the interview with each other), supervision of pilot interviews and inter-rater reliability assessment.
- Review of the cognitive debriefing results and finalisation: the findings of the debriefing process were incorporated to improve the performance of the translation. The final European Portuguese version of the CAM was a result of all the interactions described above.

Procedures

Between February and May 2012, elderly patients (≥65 years), admitted for at least 24 h into two intermediate care units (Intensive Medicine and Surgical Services) of the university hospital, CHSJ, Porto, were included in the present study. Two days per week were selected at random. Exclusion criteria were: Glasgow Coma Scale (total score ≤11) (11), blindness/deafness, inability to communicate and not able to speak Portuguese.

In the inter-rater reliability process, each researcher completed the CAM independently and separately. In the pilot study, a blind assessment was conducted by a psychiatrist (L.F.) using DSM-IV-TR (reference standard) (12) and by a psychologist (S.M.) using CAM.

The CAM was completed based on observations made during a clinical interview (patient and

family/caregiver) and a formal cognitive assessment: Mini-Mental State Examination (13) and Digit Span Test (14).

The Hospital Ethics Committee approved the present study. Informed consent was obtained from the patient or from their relatives if the patient was unable to decide for him/herself.

Data analysis

For statistical analysis, SPSS software version 19.0 was used. The inter-rater assessment reliability was calculated using Cohen's κ coefficient. The strength of agreement of the κ statistics was based on the guidelines from Landis and Koch (15).

Concurrent validity was assessed by sensitivity, specificity, positive and negative predictive value for the European Portuguese version of CAM against the reference standard, calculated by the standard formula, using 95% confidence intervals.

Results

The European Portuguese version revealed a good level of comprehensibility and conceptual equivalence with the original English version.

In the inter-rater reliability study, 26 patients were recruited, of which six were excluded (mutism). Eventually 20 were included, 20 paired tests were carried out and 40 CAM instruments were completed.

According to the guidelines from Landis and Koch (15), the inter-rater reliability was very good ($k > 0.81$) for all items and good for inattention ($k = 0.77$) and disorientation ($k = 0.65$).

In the pilot study, 77 elderly patients were initially enrolled, with 27 excluded (sixteen incomplete interviews, two refused and nine were already included in the study). The final sample ($n = 50$), with a mean age of 77.56 (SD 8.5) were majority male (60%), married (60%), with lower educational level (90% ≤ 4 years) and living at home (88%). The main reasons for hospital admission were cardiorespiratory (54%) and gastrointestinal (20%) problems.

Compared with the reference standard (DSM-IV-TR), the European Portuguese version of CAM had a sensitivity of 73% and a specificity of 95%. The positive and negative predictive values are also presented in Table 1.

The mean time between assessments was 4 h. CAM was completed in 5 min on average.

Table 1. Comparison of DSM-IV-TR diagnosis and CAM ratings

		DSM-IV-TR	
		Delirium	No Delirium
CAM	Positive	8	2
	Negative	3	37
			% [95% CI]
Sensitivity			73 [39–93]
Specificity			95 [81–99]
Positive predictive value			80 [44–96]
Negative predictive value			92 [78–98]

CAM, Confusion Assessment Method.

Discussion

The psychometric proprieties of CAM seem to be consistently good, in accordance with other validation studies (4,16–22).

The translation process was developed based on methodological assumptions that ensure its validity, well documented in each step. Despite the existence of a Brazilian Portuguese translation of the CAM, the translation and adaptation of this instrument for the European Portuguese population is necessary, bearing in mind the significant lexical, syntactical and semantic differences between the two varieties of Portuguese. Moreover, important Brazilian studies on CAM-ICU (23), an adaptation for intensive care units, have been recently published (24–26), along with a previous European Portuguese translation (27), showing the evident socio-cultural differences.

In the present study, the agreement for the nine individuals of CAM features was substantial, considering κ values.

Moderate sensitivity and good specificity were found when compared with the original study (4) and with other previous validation studies (16–22).

Delirium was incorrectly classified in two cases of moderate dementia. The differential diagnosis of delirium and dementia can be difficult because they share many common clinical features (28).

The reasons for the three false-negatives were related to fluctuations in mental state or the absence of information about the patient's cognitive baseline.

The strength of this study was linked to the inclusion of patients with dementia and other cognitive impairments and the two blind comparisons, as well as the reference standard assessment made for all patients with or without a positive CAM score.

A limitation of this study was the selection of a convenience sample, recruited from intermediate care units in the university hospital, without previously screening all of the patients admitted in these two units. In addition, a constraint in feasibility was the long interval (1–7 h) between the two assessments. Further evaluation of this version in other settings with larger sample sizes remains a task for future research.

In conclusion, the European Portuguese version of the CAM showed good feasibility and overall very good inter-rater reliability. The sensitivity and

specificity rates found also suggested that this version emerges as a promising tool in the diagnosis of delirium in elderly patients admitted into intermediate care units.

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Conflicts of Interest

None.

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VALIDATION STUDY OF THE EUROPEAN PORTUGUESE VERSION OF THE CONFUSION ASSESSMENT METHOD (CAM)

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ABSTRACT

Background: The Confusion Assessment Method/CAM is the most widely used delirium screening instrument. The aim of this study was to evaluate the reliability and validity of the European Portuguese version of CAM.

Methods: The sample included elderly patients (≥65 years), admitted for at least 48 hours, into two intermediate care units of Intensive Medicine and Surgical Services in a university hospital. Exclusion criteria were: score ≤11 on the Glasgow Coma Scale, blindness/deafness, inability to communicate and to speak Portuguese. For concurrent validity, a blinded assessment was conducted by a psychiatrist (DSM-IV-TR, as a reference standard) and by a trained researcher (CAM). This instrument was also compared with other cognitive measures to evaluate convergent validity. Inter-rater reliability was also assessed.

Results: In this sample (n=208), 25% (n=53) of the patients had delirium, according to DSM-IV-TR. Using this reference standard, the CAM had a moderate sensitivity of 79% and an excellent specificity of 99%. The positive predictive value was 95%, indicating a strong ability to confirm delirium with a positive test result, and the negative predictive value was lower (93%). Good convergent validity was also found, in particular with MMSE (r_s= -0.676; p≤0.01) and DST forward (r_s= -0.605; p≤0.01), as well as a high inter-rater reliability (diagnostic k=1.00; single items' k between 0.65 and 1.00).

Conclusion: Robust results on concurrent and convergent validity and good reliability were achieved. This version was shown to be a valid and reliable instrument for delirium detection in elderly patients hospitalized in intermediate care units.

Key words: Delirium, Aged, Confusion Assessment Method, Validation Study, Sensitivity and Specificity, Reliability.

Running title: CAM European Portuguese Version

INTRODUCTION

Delirium represents a common and severe problem among hospitalized elderly people, affecting 50% of these patients (Inouye *et al.,* 2013). This syndrome is characterized by the rapid onset of symptoms which fluctuate, a disturbance of consciousness, with reduced ability to focus, sustain or shift attention, accompanied by global disturbance of cognition or perceptual abnormalities and evidence of a physical cause, substance intoxication/withdrawal or multiple etiologies (APA, 2000).

The development of delirium in elderly people is usually multifactorial, resulting from a complex inter-relationship between vulnerable patients with several predisposing factors (e.g. dementia, multi-morbidity) and exposure to precipitating risk factors (e.g. poly-pharmacy, physical restraints) (Inouye and Charpentier, 1996).

It has also been recognized that delirium is associated with numerous negative outcomes, including increased length of hospital stay, risk of death, institutionalization and dementia (Leentjen *et al.,* 2012). Because of its clinical effects, this syndrome has important implications for healthcare utilization and costs, amounting to over 182 billion dollars per year in 18 European countries (including Portugal) (Inouye *et al.,* 2013).

Despite this, delirium is often unrecognized, with non-detection rates as high as 69%. Failure to diagnose delirium potentially compromises patient safety and may have downstream implications for clinical care and patient health, delaying identification and treatment of underlying medical illness (Inouye *et al.,* 2001; McLafferty and Farley, 2007).

Some studies have identified factors associated with unrecognized delirium. One of them (Inouye *et al.,* 2001), identified four independent risk factors: hypoactive delirium, advanced age, vision impairment and dementia. Patients with 3 or 4 risk factors had a 20-fold risk of under-recognition. Some other factors have also been identified: the fluctuation course of delirium symptoms, the lack of knowledge about delirium and its identification, as well as the failure to consistently use standardized screening instruments in daily clinical practice (Inouye, 2006). Most health professionals

recognize that delirium is a seriously under-diagnosed problem, but only a minority routinely screens for delirium and few use a specific tool for assessment (Ely *et al.,* 2004).

The use of these instruments in clinical practice can help not only in the detection of delirium, but also in rating clinical improvement and evaluating the effectiveness of various interventions (Grover and Kate, 2012), contributing to the enhancement of patient outcomes and a decrease in the associated burden (Hughes *et al.,* 2012).

Therefore, a variety of screening tools have been developed. Among them, the Confusion Assessment Method/CAM (Inouye *et al.,* 1990) has been considered to be the most useful diagnostic or screening instrument for several reasons, including its brevity, and ease of use by trained non-psychiatric clinicians in both clinical and research settings (Wong *et al.,* 2010).

It was originally developed based on the DSM-III-R criteria (APA, 1987), assessing the presence, severity and fluctuation of nine clinical features: acute onset and fluctuating course*, inattention*, disorganized thinking*, altered level of consciousness*, disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation, and altered sleep–wake cycle. This instrument also includes a diagnostic algorithm (short version), based on the four cardinal features of delirium (previously marked with an asterisk). Delirium diagnosis requires the presence of features 1 and 2, and either 3 or 4. This instrument also had a severity score based on the shortened version, with higher scores indicating increased severity (Inouye, 2003). In the original study (Inouye *et al.,* 1990), the CAM was validated against psychiatric diagnosis, showing high levels of sensitivity (94%-100%), specificity (90%-95%), and positive (91-94%) and negative predictive values (90%-100%). It was also found to have good convergent validity with other cognitive measures (e.g. MMSE and DST), and high inter-rater reliability (k=0.81- 1.00).

The CAM has become the most widely-used instrument (Wei *et al.,* 2008), recommended by the most recent guidelines (NICE, 2010). It has been used in more

than 4000 published studies so far and translated into at least 12 languages (Inouye *et al.,* 2013). The aim of this study is to present the reliability and validity of the European Portuguese version of CAM (long version).

METHODS

Translation Process and Pilot-Study

The CAM was translated in accordance with standard translation guidelines of ISPOR (Wild *et al.,* 2009), which also included trained researchers, according to the original training manual (Inouye, 2003). Following this, the European Portuguese version of CAM was tested in a pilot-study, with 50 elderly patients, recruited from the same clinical settings where the present study was carried out. It was found to have a good level of comprehensibility, inter-rater reliability (k>0.81), as well as moderate sensitivity (73%) and excellent specificity (95%). These preliminary results suggested that this version showed good ecological, face and content validity. Supporting data are described in greater detail in a previous publication (Martins *et al.,* 2012).

Sample

The sample included elderly patients (≥65 years), who had been admitted for at least 48 hours, into two intermediate care units (IMCU) of Intensive Medicine and Surgical Services in the university hospital (CHSJ), in Porto. Two days per week were selected at random. The exclusion criteria were: a total score ≤11 on the Glasgow Coma Scale (Teasdale and Jennett, 1974), blindness/deafness, inability to communicate and to speak Portuguese.

Procedures

All patients included were assessed by a trained researcher (SM), who completed CAM based on observations made during a clinical interview and a formal cognitive assessment, with the Mini-Mental State Examination/MMSE (Folstein *et al.,* 1975)

(cognitive global measure) and Digit Span Test/DST (Wechsler, 1997) (attention and work memory measure). The CAM was completed immediately after the interview to ensure accurate information. The patient's family or caregivers and nurses, were also interviewed about the patient's prior cognitive performance and any recent cognitive change.

Delirium severity was determined using the scoring system of the CAM algorithm. It was solely used for the purpose of calculating the correlations between CAM and other cognitive instruments.

The CAM interviewer had limited information concerning the patient and was blinded to the patient's medical records.

The reference standard for delirium was also assessed in all patients by one of the authors (LF), an experienced geriatric psychiatrist, according to the DSM-IV-TR criteria (APA, 2000). This assessment comprised a patient clinical interview, mental status examination, family and nurse interviews, as well as a review of medical records.

These two assessments were independent and blinded, and were performed in most of the cases an average of 4 hours apart from each other (between 1 to 6 hours).

The inter-rater reliability analysis was carried out in a convenience sample of 40 patients, recruited only from the IMCU of the Intensive Medicine Service. Patients were interviewed by a trained psychologist (SM) and nurse (CL). The order of the interview was alternated. Both raters completed the CAM independently on the basis of their observations during the interview, blinded to each other. Test-retest was not performed due to the fluctuating course of this syndrome.

Complete demographic and clinical characteristics of patients and hospital-related data were also obtained through chart review. The sample was also described with regard to the presence or absence of cognitive impairment/dementia, based on doctors' information registered in the medical records.

The Ethics Committee of the Hospital approved the study. Informed consent was obtained from the patient or their closest relative, if the patient was unable to decide for

him/herself.

Statistical Analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences Version 21.0 for Windows software (SPSS).

Patient characteristics are presented as raw frequencies and percentages for categorical variables and as median, minimum and maximum for continuous variables, as normality could not be assumed.

For analysis of differences between the two groups with and without delirium (according DSM-IV-TR criteria), the Mann-Whitney test for continuous variables, Chi-square test for paired categorical variables and Fisher's exact test for dichotomous variables were used at a significance level of 0.05.

Concurrent validity was assessed by sensitivity, specificity, positive and negative predictive values, as well as likelihood ratio for the European Portuguese CAM against the reference standard (DSM-IV-TR criteria), calculated by standard formula, using 95% confidence intervals (CI).

Convergent validity was explored by calculating Spearman's p rank correlation coefficients between CAM severity score and total scores for MMSE and Digit Span Test (forward and backward), at a significance level of 0.01.

Inter-rater reliability was calculated using Cohen's kappa coefficient, for each feature in the instrument. The strength of agreement of the kappa statistics was based on the guidelines from Landis and Koch (1977), which defined $k>0.61$ as substantial and $k>0.81$ as almost perfect.

RESULTS

Between June 2012 and June 2013, 268 patients were enrolled in this study, of whom 20 refused to participate, 16 had already been included, 11 were excluded due to an incomplete interview (mainly due to care management or clinical procedures) and 10

who were in terminal condition, with 3 dying during the study period.

The final sample included 208 elderly patients, most of them (75.5%) recruited from the IMCU of the Intensive Medicine Service. The sociodemographic characteristics of the sample are presented in Table 1, and did not differ significantly between the groups with and without delirium, classified by DSM-IV-TR criteria. In relation to the clinical characteristics (Table 2), significant differences were noted for admission type ($p=0.008$) and length of stay in the IMCU ($p<0.001$), with the delirium group presenting the highest duration of hospitalization. As expected, significant differences regarding total scores of MMSE ($p<0.001$), Digit Span forward ($p<0.001$) and backward ($p<0.001$) were found, with the lowest values in the delirium group. There was also a verified difference for the total number of co-morbidities, revealing a fairly higher value ($p=0.049$) in the group without delirium. The most common reasons for admission were cardiorespiratory and gastrointestinal problems, with no significant differences found between groups or for the number of daily medications.

Concurrent validity

The occurrence rate of delirium was 25% (n=53), according to the reference standard DSM-IV-TR rating. In these patients, only 42 were also positive according to the CAM. The CAM rated 153 of the 155 patients negatively whom the psychiatrist also rated as not being delirious.

Using DSM-IV-TR as a reference standard, the CAM had a sensitivity of 79% and a specificity of 99%. The positive predictive value of the test in the sample was 95%, indicating a strong ability to confirm delirium with a positive test result, and the negative predictive value was lower (93%). A kappa statistic of 0.83 (CI95% 0.74-0.92) was found between the CAM and DSM-IV-TR.

Convergent validity

Negative correlations between CAM severity score and the total of the MMSE ($r_s= -0.676$; $p\leq0.01$), Digit Span Test forward ($r_s= -0.605$; $p\leq0.01$) and backward ($r_s= -0.487$; $p\leq0.01$) were found.

Inter-rater reliability

In the inter-rater reliability, the total CAM algorithm and five clinical features presented k=1.00.The k values for the other clinical features are presented in Table 4. In this study, the median time for the CAM interviews (with cognitive measures) was 20 minutes and for completion of CAM ratings, 5 minutes.

DISCUSSION

This study clearly indicates that the European Portuguese version of CAM has good reliability and validity, with robust positive data on concurrent and convergent validity and inter-rater reliability.

Moderate sensitivity and excellent specificity were found, when compared with the original study (Inouye *et al.,* 1990), as well as with other previous validation studies (Fabbri *et al.,* 2001; Monette *et al.,* 2001; Laurila *et al.,* 2002; Gonzalez *et al.,* 2004; Hestermann *et al.,* 2007; Ryan *et al.,* 2009; Wongpakaran *et al.,* 2011). However, there is some heterogeneity in the methodological issues in these studies, regarding the setting, sample, cognitive assessment tools used and formal trainer researchers. In addition, some of them did not consider the inclusion of patients with dementia, depression or other psychiatric disorders (Rockwood *et al.,* 1994, Pompei *et al.,* 1995, Rolfson *et al.,* 1999, Gonzalez *et al.,* 2004), who are easily confused with delirious patients. This can explain some higher values in sensitivity. In fact, any test can distinguish the severely diseased from the healthy, but more important is the test's ability to distinguish confounding cases (Jaeschke *et al.,* 1994). So, in this setting with a high prevalence of confounding factors diagnoses, a sensitivity of 79% can still be appreciated as being very good.

Two false-positives and eleven false-negatives were found. With dementia present, health professionals often overcalled delirium in dementia patients (Inouye *et al.,* 2005), due to the overlap of several features, which makes differential diagnosis more complex (Inouye, 2006). This can explain the two false-positive cases verified where

delirium was incorrectly classified in the patients with moderate dementia.

On the other hand, health professionals also frequently misattributed delirium symptoms to underlying dementia (Inouye *et al.,* 2005). This appears as the main reason for four of the eleven false-negative ratings found. Determining whether a patient has delirium, delirium superimposed on preexisting neurocognitive disorder or a major neurocognitive disorder separate from delirium (such as dementia) is a major challenge for clinicians. This is complicated as these disorders frequently coexist. One study found that the frequency of delirium in patients hospitalized with dementia was as high as 89% (Fick *et al.,* 2002). Moreover, dementia is a leading risk factor for delirium (Inouye *et al.,* 2013) and, conversely, delirium seems to create an increased vulnerability to the development of dementia (Witlox *et al.,* 2010) and also contributes to the acceleration of cognitive decline in patients with dementia (Fong *et al.,* 2009).

In the present study, delirium symptoms were also misattributed to depression in one patient, and not detected in another patient with visual and hearing impairment, which is in agreement with the results of previous studies (Farrell *et al.,* 1995; Inouye *et al.,* 2001).

As delirium can rapidly fluctuate, the extensive interval (6 hours) in five cases may have caused some discordant observations between research and psychiatric assessment. This discordant result may not be a reflection of the test characteristics but rather an implication of the fluctuating nature of delirium itself. Fluctuation is an intrinsic problem of studying delirium (McNicoll *et al.,* 2005).

In the present study, a good agreement between CAM and DSM-IV-TR was found, according to the guidelines from Landis and Koch (1977).

Regarding the convergent validity, a significant inverse relationship was observed between the CAM severity score and other cognitive measures, particularly with MMSE and DST forward, which supports the detrimental effect of delirium on cognition (Voyer *et al.,* 2007).

In this study, inter-rater reliability was excellent, with an agreement of 100% (k=1.00)

for the diagnosis of delirium and for the majority of the individual items (at least five). However, the disorganized thinking item presented the lowest value (k=0.65), which was described as k=1.0 in the original study (Inouye *et al.,* 1990), without further discussion. This result might suggest that the scrutiny of cognitive measures performance was not sufficient. The addition of some standardized questions or specific tasks, such as interpretation of proverbs or description of similarities and differences between words, which requires organized, rational, conceptual thinking, could probably enhance the assessment of this clinical feature. Another additional explanation could be the different backgrounds of the two raters (psychology/nursing), which may also have contributed to some disagreements.

The present study has some strengths. First, appropriate training of the interviewers and a formal cognitive assessment (in particular with an attention measure) were performed before the CAM rating. Second, the comparisons between raters were blind and were made for all patients independently of whether or not they had delirium according the CAM. Third, the study population represents patients for whom testing by the European Portuguese version of CAM in a clinical "real-life" setting would be useful, once they presented high risk (e.g. advanced age, dementia) for development of this syndrome. Moreover, despite the increased number of intermediate care units in hospitals, there are few data in the literature regarding delirium in this context, compared to the information on critically ill patients.

A limitation in the present study was the selection of a convenience sample, recruited from intermediate care units in the referred hospital, without previous screening all of the patients admitted in these two units.

In addition, some patients were not interviewed within a shorter time interval, due to technical reasons, clinical circumstances and the care management needed in the units.

On the other hand, as this is a two-site study, validation of the performance of this instrument will be required in other settings to assure generalizability. Further research

should focus on the use of this instrument in various settings by different levels of health professionals.

Using the MMSE and DST in order to rate the CAM could be difficult for routine ward nurses who are already very busy with clinical duties. In these cases, when time is scarce, assessment with other brief instruments (e.g. Abbreviated Mental Test) and attention tasks (e.g. Digit Span Test or listing days of the week backwards) can be alternatively used (Inouye *et al.,* 2013).

In Portugal, standardized assessment of delirium is still scarce and no national strategy for routine monitoring, prevention or treatment of this syndrome exists. The implementation of the European Portuguese version of CAM in daily practice is feasible and could lead to raised awareness in health care professionals. Besides that, CAM is an internationally recognized and used scale, so another important benefit of this validated version is that it can be used as a tool for multinational clinical research and comparison with other countries.

The European Portuguese version of the CAM has been shown to be a valid and reliable instrument for delirium detection in elderly patients hospitalized in intermediate care units by non-psychiatric trained health professionals and could be a valuable tool for future studies, namely on delirium incidence, risk factors and outcomes.

Conflict of Interest: none.

Description of authors' roles: Lia Fernandes and Mário R. Simões participated in the definition and design of the study. Sónia Martins, Carla Lourenço and Lia Fernandes participated in the data collection and the writing the article. Sónia Martins, Mário R. Simões and Lia Fernandes contributed to the analyses and interpretation of the results, as well as to the critical revision of the article with João Pinto-de-Sousa, Filipe Conceição and José Artur Paiva. All authors have approved the final manuscript.

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Table 1 - Demographic characteristics of sample

Characteristics	Overall (n=208)	Delirium (n=53)	No delirium (n=155)	*p*-value
Age, median (min.-max.)	78 (65-98)	79 (65-95)	77 (65-98)	0.306[(1)]
Education, years, median (min.-max.)	4 (0-17)	3 (0-17)	4 (0-17)	0.142[(1)]
Gender, n (%)				
Female	112 (53.8)	25 (47.2)	68 (43.9)	0.259[(2)]
Male	96 (46.2)	28 (52.8)	87 (56.1)	
Marital status, n (%)				
Single	10 (4.8)	2 (3.8)	8 (5.2)	
Married	111 (53.4)	34 (64.2)	77 (49.7)	0.329[(3)]
Divorced/separated	8 (3.8)	1 (1.9)	7 (4.5)	
Widowed	79 (38.0)	16 (30.1)	63 (40.6)	
Living situation, n (%)				
Alone	40 (19.2)	5 (9.4)	35 (22.6)	
With partner	86 (41.3)	24 (45.3)	62 (40.0)	
With son or daughter	47 (22.6)	15 (28.3)	32 (20.6)	
With partner and son/daughter	17 (8.2)	5 (9.4)	12 (7.8)	0.328[(3)]
With other relatives	8 (3.8)	1 (1.9)	7 (4.5)	
Others	10 (4.9)	3 (5.7)	7 (4.5)	
Place of living/care, n (%)				
Home	197 (94.7)	50 (94.3)	147 (94.8)	1.000[(4)]
Nursing home	11 (5.3)	3 (5.7)	8 (5.2)	
Has a carer? n (%)				
Yes	120 (60.9)	30 (66.7)	90 (59.2)	0.368[(2)]
No	77 (39.1)	15 (33.3)	62 (40.8)	
Caregiver relationship, n (%)				
Son or daughter	52 (43.3)	17 (56.7)	35 (38.9)	
Spouse	23 (19.2)	7 (23.3)	16 (17.8)	0.108[(2)]
Other relative	17 (14.2)	1 (3.3)	16 (17.8)	
Friend	28 (23.3)	5 (16.7)	23 (25.5)	

[(1)]Mann-Whitney test;[(2)]Chi-Square Independent test;[(3)]Chi-square's exact test;[(4)]Fisher's exact test; min.-minimum; max.-maximum.

Table 2 - Clinical characteristics of sample

Characteristics	Overall (n=208)	Delirium (n=53)	No delirium (n=155)	*p*-value
Admission type, n (%)				
Emergency department	123 (59.7)	24 (45.3)	99 (64.7)	**0.008**[(3)]
Operating room	43 (20.9)	10 (18.9)	33 (21.6)	
Inter-hospital transfer	27 (13.1)	12 (22.6)	15 (9.7)	
Intensive care units	8 (3.9)	5 (9.4)	3 (2.0)	
Wards	5 (2.4)	2 (3.8)	3 (2.0)	
Reason for admission, n (%)				
Cardiorespiratory	92 (44.2)	17 (32.1)	75 (48.5)	0.246[(3)]
Gastrointestinal	43 (20.7)	14 (26.4)	29 (18.7)	
Urology/nephrology	30 (14.5)	7 (13.2)	23 (14.8)	
Cancer	19 (9.1)	5 (9.5)	14 (9.0)	
Neurology	8 (3.8)	4 (7.5)	4 (2.6)	
Fall	9 (4.3)	4 (7.5)	5 (3.2)	
Other	7 (3.4)	2 (3.8)	5 (3.2)	
IMCU length of stay (days), median (min.-max.)	7 (3-36)	8 (4-36)	6 (3-34)	**<0.001**[(1)]
Total of co-morbidities, median (min.-max.)	7 (0-16)	6 (2-14)	7 (0-16)	**0.049**[(1)]
Medication (daily)**,** median (min.-max.)	7 (0-16)	6 (0-16)	7 (0-16)	0.170[(1)]
Poly-medication, n (%)				
Minor ≤4	56 (27)	17 (33.3)	39 (25.5)	0.277[(2)]
Major ≥5	148 (73)	34 (66.7)	114 (74.5)	
MMSE (total), median (min.-max.)	17 (0-30)	7 (0-22)	20 (0-30)	**<0.001**[(1)]
Digit span test (total), median (min.-max.)				
Forward	5 (0-12)	3 (0-6)	6 (0-12)	**<0.001**[(1)]
Backward	1 (0-8)	0 (0-4)	2 (0-8)	**<0.001**[(1)]

[(1)]Mann-Whitney test; [(2)]Chi-Square Independent test; [(3)]Chi-square's exact test; max.-maximum; IMCU – Intermediate Care Unit.

Table 3 – Comparison between CAM and DSM-IV-TR

	DSM-IV-TR
CAM	% [95% CI]
Sensitivity	79 [65-88]
Specificity	99 [94-99]
Positive predictive value	95 [83-99]
Negative predictive value	93 [88-96]
Likelihood ratio for positive test	61 [15-245]
Likelihood ratio for negative test	0.21 [0.12-0.36]

95% CI = 95% confidence interval

Table 4 – Inter-rater reliability

Item	***k* [CI 95%]**
1. Acute onset	1.00 [1.00-1.00]
2. Inattention	0.78 [0.52-1.02]
3. Disorganized thinking	0.65 [0.38-0.92]
4. Altered level of consciousness	1.00 [1.00-1.00]
5. Disorientation	0.79 [0.63-0.96]
6. Memory impairment	0.83 [0.68-0.99]
7. Perceptual disturbances	1.00 [1.00-1.00]
8. a) Psychomotor agitation	1.00 [1.00-1.00]
b) Psychomotor retardation	0.73 [0.50-0.95]
9. Altered sleep-wake cycle	1.00 [1.00-1.00]

k = Cohen´s *k* coefficient; 95% CI = 95% confidence interval

Footnote: For inter-rater reliability analysis, forty elderly patients were included. The majority were female (53%), married (53%), with a low educational level (90% 0-4 years of education) and with a mean age of 78.5 (sd=6.9). The main admission reasons were cardiorespiratory (50%) followed by urology/nephrology problems (23%).

3.3. Family in the Delirium Recognition: European Portuguese Validation Study of the Family Confusion Assessment Method (FAM-CAM). Martins S, Conceição F, Paiva JA, Simões MR, Fernandes L. Journal of the American Geriatrics Society, 2014: 1-5. First published online: 15 Jul 2014.

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Delirium Recognition by Family: European Portuguese Validation Study of the Family Confusion Assessment Method

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OBJECTIVES: To present the validation study of the European Portuguese version of the Family Confusion Assessment Method (FAM-CAM) and to assess the level of psychological distress in families and caregivers of elderly hospitalized adults with delirium.

DESIGN: Validation study.

SETTING: Intermediate care unit of the Intensive Medicine Service of the São João Hospital Center, Porto, Portugal.

PARTICIPANTS: Families and caregivers of elderly hospitalized adults (≥48 hours). Inclusion criteria were sufficient knowledge about the individual to enable reporting on his or her mental and physical abilities and staying at the individual's bedside daily during hospitalization. Families and caregivers younger than 18 and those who did not speak Portuguese were excluded.

MEASUREMENTS: A trained researcher translated the FAM-CAM according to International Society For Pharmacoeconomics and Outcomes Research guidelines. All individuals were assessed using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) (reference standard) and the Confusion Assessment Method (CAM). A trained researcher administered the FAM-CAM to families and caregivers. The level of family-perceived distress was evaluated on a numerical rating scale from 0 to 4.

RESULTS: The sample included 40 families and caregivers (58% adult children). According to the DSM-IV-TR, 20% of individuals had delirium. The FAM-CAM had moderate sensitivity (75%) and good specificity (91%) when assessed against the DSM-IV-TR and better sensitivity (86%) and specificity (91%) than the CAM. Fifty-seven percent of families and caregivers classified delirium as an extremely distressing experience.

CONCLUSION: These preliminary results suggest that FAM-CAM is a sensitive screening tool for family detection of delirium in elderly hospitalized adults. The high level of psychological distress found corroborated previous studies. Future studies with larger samples will be needed for further validation and to allow the analysis of other psychometric properties. **J Am Geriatr Soc 2014.**

Key words: delirium; aged; FAM-CAM; validation study; family caregivers

Delirium is a complex neuropsychiatric syndrome with acute onset and fluctuating course described as a disturbance of consciousness with reduced ability to focus or sustain or shift attention accompanied by cognitive deficits or perceptual disturbances. The etiologies of delirium are often multifactorial and are due to an underlying medical condition, medication effects, and substance abuse.[1,2]

Delirium is a potentially preventable clinical syndrome that occurs frequently in elderly hospitalized adults. Its occurrence has been associated with negative prognostic implications, including longer hospital stay, risk of death, institutionalization, and dementia, and imposes a significant burden on the healthcare system and society.[3–5]

Despite the potential benefits of early detection and prompt treatment, delirium is consistently underdiagnosed in clinical practice, which has been explained according to several factors, such as its fluctuating course and its overlap with dementia. A lack of adequate information regarding premorbid level of cognition and functionality in the individual can also contribute to missing the diagnosis.[6,7]

Taking this into account, when shared with health professionals, the information that families and caregivers have about an individual's previous mental state and their

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observations on mental status changes can play an important role in the assessment of some features of delirium (namely onset and fluctuating course) and can contribute to a differential diagnosis with dementia.[8,9] In a previous study[10] of delirium assessment in individuals with dementia, family members noted changes in mental status in all participants, compared with only 22% of clinical staff, although the use of observation forms or standardized assessment instruments to achieve this information is recommended.[11]

In this context, the Family Confusion Assessment Method (FAM-CAM)[12,13] was derived from the original Confusion Assessment Method (CAM) instrument[14] to screen for delirium by interviewing family caregivers with specific questions about new or sudden changes in activity and the behavioral and cognitive status of their relative. In the original study,[13] with a sample of caregivers of elderly adults with preexisting cognitive impairment, FAM-CAM showed good sensitivity and specificity.

More recently, the Informant Assessment of Geriatric Delirium (I-AGeD),[15] a new caregiver-based 10-item questionnaire, was constructed based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) criteria[1] and on an expert panel. In spite of I-AgeD's ease of use, its sensitivity and specificity vary from fair to high depending on the presence of comorbid dementia.

Despite the benefit of involving family in the detection of delirium, it is also important to recognize that delirium can be a psychologically traumatic experience, not only for individuals, but also for their families and caregivers.[16] Several studies have reported that family members had high levels of distress, even higher than health professionals and individuals reported because their distress was associated with several factors, such as the presence of psychomotor agitation and psychotic symptoms.[11,17,18]

The main aim of this study was to present the validation study of the European Portuguese version of the FAM-CAM. A second aim was to assess the level of psychological distress in families and caregivers of elderly hospitalized adults with delirium.

METHODS

Translation Process

The FAM-CAM was translated according to standard translation guidelines suggested by The Translation and Cultural Adaptation Group of The International Society For Pharmacoeconomics and Outcomes Research,[19] which include obtaining the copyright clearance from the author for use and translation; forward translation of the original instrument into Portuguese independently by two translators who are health professionals; reconciliation of the two forward translations into a single translation; back translation to English by an independent professional without any information about the original version; back translation review and harmonization by comparing the versions to detect any translation discrepancies and to ensure conceptual equivalence between versions; cognitive debriefing by testing the alternative wording, the level of comprehensibility, interpretation, and cultural relevance of the translation on a group of five family caregivers from the target population; and review of the cognitive debriefing results and finalization—the final version of all of the steps described above. This process also involved a trained researcher, according to the recommendations from the original manual.[12] The European Portuguese translation of the FAM-CAM is covered under the original copyright and can be obtained from the Hospital Elder Life Program website (http://www.hospitalelderlifeprogram.org).

Sample

This study was conducted with a sample of families and caregivers of elderly adults hospitalized (≥48 hours) in an intermediate care unit of the Intensive Medicine Service, São João Hospital Center, Porto, Portugal.

Inclusion criteria were sufficient knowledge about the individual to enable reporting on his or her mental and physical abilities and staying at the individual's bedside daily during hospitalization (≥2 days). Families and caregivers younger 18 years and who did not speak Portuguese were excluded.

Procedures

Delirium was operationally defined according to the DSM-IV Text Revision (TR) criteria (as criterion standard),[20] as assessed by a psychiatrist (LF). This assessment comprised a clinical interview, mental status examination, cognitive assessment (using the Mini-Mental State Examination (MMSE)), family and nurse interviews, and a review of medical records.

A trained researcher (SM), who completed the European Portuguese Version of the CAM (long version)[21] based on observations made during a clinical interview and a formal cognitive assessment with the MMSE (cognitive global measure) and Digit Span Test (DST) (attention and work memory measure) blinded and independently evaluated all individuals on the same day. The CAM was completed immediately after the interview to ensure accurate information.

After this, the researcher administered the FAM-CAM to the family and caregiver, reading the items and the answer options exactly as written. Following recommendations in the FAM-CAM manual,[12] the researcher (SM) made it clear to the families that the questions referred to recent, new, or sudden changes only, so no additional information or examples were given apart from those contained in the FAM-CAM itself.

Demographic and clinical information about individual, family, and caregiver characteristics was also collected.

The hospital ethics committee approved the study. Informed consent was obtained from the individuals or their relatives.

MEASURES

Confusion Assessment Method

The CAM[14] is a widely used delirium screening instrument developed to provide a standardized method to enable non-psychiatric-trained clinicians to identify delirium quickly and accurately in clinical and research settings.

This instrument included nine criteria (long version) of the DSM, Third Edition, Revised (III-R),[1] including the four cardinal features (short version): (i) acute onset and fluctuating course, (ii) inattention, (iii) disorganized thinking, and (iv) altered level of consciousness. A diagnosis of delirium requires the presence of features (i), (ii), and (iii) or (iv). The other features are disorientation, memory impairment, perceptual disturbances, psychomotor agitation and retardation, and altered sleep–wake cycle.

In the original study,[14] CAM demonstrated a high interrater reliability (k = 0.8–1) and good convergent validity with other cognitive measures, and in validation against geriatric psychiatrist assessments (using DSM-III-R criteria), it had a sensitivity of 94–100% and a specificity of 90–95%.

The FAM-CAM

The FAM-CAM[12,13] includes 11 questions directed to a family member for assessment of the four cardinal features of delirium (mentioned above) and inappropriate behavior and perceptual disturbances, such as hallucinations. These characteristics, although uncommon in delirium, were included in this instrument to maximize sensitivity and specificity.

Delirium is suggested if acute onset or fluctuating course, inattention, and disorganized thinking or an altered level of consciousness are present. Further clinical and cognitive assessment of the participant with a formal delirium rating should follow a positive result on the FAM-CAM. A health professional with previous training including previous practice with the CAM should administer this instrument, based on the original manual. It can be administered to a caregiver in person, on the telephone, or electronically, allowing the delirium assessment to take place in a wide range of settings.[12]

Psychological Distress

Only when FAM-CAM and clinical diagnosis according to the reference standard were both positive was the level of family-perceived distress evaluated. This assessment was performed after delirium resolution with the question: "How distressing was the individual's delirium for you?" (0 = no distress at all to 4 = extremely distressing).

Statistical Analysis

Statistical analyses were performed using SPSS version 21.0 for Windows (SPSS, Inc., Chicago, IL). Individual, family, and caregiver characteristics are presented as raw frequencies and percentages for categorical variables and as median and range for continuous variables because normality could not be assumed.

For analysis of differences between the groups (with and without delirium), the Mann–Whitney test was used for continuous variables, the chi-square test for paired categorical variables, and the Fisher exact test for dichotomous variables, at a significance level of .05. Concurrent validity was assessed for sensitivity, specificity, positive predictive value, and negative predictive value for the European Portuguese version of the FAM-CAM against the reference standard (DSM-IV-TR) and the CAM using 95% confidence intervals. The Cohen *k* coefficient was used to calculate agreement between the raters. The strength of agreement was based on previously developed guidelines.[22]

RESULTS

The European Portuguese version of the FAM-CAM had a good level of comprehensibility and conceptual equivalence with the original English version.

This study included 40 families or caregivers, with a mean age of 55 ± 15. Most were adult children (58%), female (70%), married (80%), and employed (53%) and had a low education level (40% 0–4 years). The majority were the main caregiver (68%), and the mean duration of contact with the individual during hospitalization until the FAM-CAM assessment was 5 ± 3 days. The main sociodemographic and clinical characteristics of the participants are presented in Table 1. These characteristics did not differ significantly between the groups with and without delirium, classified using the DSM-IV-TR criteria, but the group with delirium had fewer years of education. Previous studies[23,24] had referred to education as an important risk factor for delirium, which may partially explain this result.

Table 1. Demographic and Clinical Characteristics of Elderly Adults

Characteristics	Overall (n = 40)	Delirium Positive (n = 8)	Delirium Negative (n = 32)	*P*-Value
Age, median (range)	80 (66–93)	80 (67–88)	80 (66–93)	.93[a]
Education, years, median (range)	4 (0–12)	0 (0–4)	4 (0–12)	.02[b]
Sex, n (%)				
Female	26 (65)	5 (63)	21 (66)	>.99[b]
Male	14 (35)	3 (38)	11 (34)	
Marital status, n (%)				
Married	18 (45)	5 (63)	13 (41)	.55[c]
Divorced or separated	1 (3)	—	1 (3)	
Widowed	21 (53)	3 (38)	18 (56)	
Reason for admission, n (%)				
Cardiorespiratory	14 (35)	2 (25)	12 (38)	.67[c]
Urological or nephrological	11 (28)	3 (38)	8 (25)	
Gastrointestinal	9 (23)	1 (13)	8 (25)	
Cancer	1 (3)	—	1 (3)	
Neurological	2 (5)	1(13)	1 (3)	
Fall	2 (5)	1(13)	1 (3)	
Other	1 (3)	—	1 (3)	
Caregiver relationship, n (%)				
Son or daughter	23 (58)	2 (25)	21 (66)	.10[c]
Spouse	9 (23)	4 (50)	5 (16)	
Other relative	6 (15)	2 (25)	4 (13)	
Friend	2 (5)	—	2 (6)	

[a]Mann-Whitney test.
[b]Fisher exact test.
[c]Chi-square exact test.

According to the DSM-IV-TR, eight (20%) participants had delirium. The FAM-CAM classified six of these correctly. FAM-CAM ratings were negative for 29 of the 32 participants rated as not having delirium according to the DSM-IV-TR. Compared with the reference standard DSM-IV-TR and the CAM, the FAM-CAM had a sensitivity of 75% and 86%, respectively, and a specificity of 91%. The positive and negative predictive values are presented in Table 2. Based on previously developed guidelines,[22] agreement between the FAM-CAM and the DSM-IV-TR ($k = 0.6$, 95% CI = 0.3–0.9) and CAM ($k = 0.7$, 95% CI = 0.4–1.0) was substantial.

All family members found delirium to be a distressing experience (57% indicating 4 (extremely distressing) on the Likert scale).

DISCUSSION

Globally, the European Portuguese version of the FAM-CAM had good psychometric properties. Compared with the results found in the original study,[13] this version had slightly lower sensitivity (88–86%) and in particular less specificity (98–91%) than the CAM, although some methodological differences between these studies should be taken into consideration, such as where the test was conducted, the sample used, and which FAM-CAM was filled (caregiver vs research and clinical staff). In the original study,[13] 52 dyads of elderly adults with preexisting cognitive impairment and their family caregivers were included. These were drawn from two primary studies: the eCare for Eldercare pilot study[25] and the Hospital to Home study.[26] As mentioned above, the present research was conducted with a sample of elderly hospitalized adults (with and without previous cognitive impairment) and their families and caregivers. In the original study, the family caregiver completed the FAM-CAM daily at home and at visits after hospital discharge. These caregivers had previously been trained in understanding symptoms of delirium and how to score the FAM-CAM. In the present research, the research assistant administered this instrument to the family member.

Nevertheless, this first study to validate the FAM-CAM against a reference standard (DSM-IV-TR) for delirium found moderate sensitivity and good specificity.

More false-positives (n = 3) than false-negatives (n = 2) were found when than FAM-CAM was compared with the DSM-IV-TR and the CAM.

Table 2. Comparison of the Family Confusion Assessment Method (FAM-CAM), *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR), and the Confusion Assessment Method (CAM)

	DSM-IV-TR	CAM
FAM-CAM	% (95% Confidence Interval)	
Sensitivity	75 (35–95)	86 (42–99)
Specificity	91 (74–97)	91 (74–97)
Positive predictive value	67 (31–91)	67 (31–91)
Negative predictive value	93 (77–99)	97 (81–99)

The fluctuating course of delirium, with disturbances frequently more evident in the evening,[27] when families are not with the hospitalized individual, can explain the two false-negatives, although in one of these cases, the participant had moderate dementia, which is difficult to differentiate from delirium.[7]

The overinterpretation of delirium symptoms by family and caregivers can explain in part the three false-positive cases. Previous studies[11,17] have indicated that families identify more delirium-related symptoms than health professionals; anxiety related to their relative's acute illness and the course of the hospitalization and the discharge plans can affect their identification and recall.

Nevertheless, in some cases, a family member, when asked the right questions, may be better at identifying symptoms of delirium than trained clinicians or research staff, given their intimate knowledge of the individual's baseline. They can offer valuable information regarding individual baseline status and can potentially monitor behavior and even the response to some treatment.[11,28,29] Information from families and caregivers can also be helpful in detecting delirium in outpatient settings. Some studies have found evidence that a significant proportion of these individuals do not recover from delirium, presenting persistent symptoms at discharge or beyond. Close clinical follow-up after discharge is crucial, especially because of the poor outcomes associated with delirium.[27]

Needs and stress of family members required recognition and minimization,[16] in particular, when they observed a relative during an episode of delirium. In the present study, even with the low number of family members assessed, more than half considered delirium as an extremely distressing experience. Previous studies have found an even higher level of distress.[11,17,18] In this way, providing support and education can help families throughout this process, as well as encouraging them to share their experiences. Moreover, family/caregivers' education programs can be beneficial in improving management and alleviating psychological distress.[7,29,30]

One strength of the present study was the use of an external criterion standard. In addition, the study sample included people at high risk of developing delirium: advanced age, acute illness, and cognitive impairment. In this case, the use of the FAM-CAM would be useful for the detection of this syndrome, although it cannot be used as an independent diagnostic instrument without clinical confirmation.

The convenience sample recruited from a single intermediate care unit, as well as its small size, limits generalizations that may be made from the results. Furthermore, the study of the level of distress was limited because of the number of delirium cases, and no correlations between these levels and individual and family characteristics was possible. In addition, interrater reliability was not evaluated. Finally, it would be of great interest to compare the present results with those of the I-AGeD, which was developed recently and has no Portuguese version available.

Given that delirium is often undetected, it is important to optimize the information gathering from all available sources, including family and caregivers, by using validated standardized instruments. This may contribute to improvement in early delirium recognition and adverse outcomes associated with delirium. In spite of this, the role of family

in the assessment, as well as in prevention interventions and management of this syndrome, has received limited formal study.[15,28]

The results of the present study suggest that the European Portuguese version of the FAM-CAM is a sensitive family screening tool for detection of delirium in elderly hospitalized adults, but future studies with larger samples from other clinical settings will be needed to validate these results. This version should also be tested against delirium and cognitive scales other than the CAM. Direct comparison with the I-AGeD will also be an important area for future work. The evaluation of an alternative administration method may be useful, with family caregivers completing the FAM-CAM, in particular with community-dwelling elderly people. Future research into the expertise that family members can offer to clinicians and its effect on the detection and management of this syndrome will be needed.

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4. CONCLUSÃO

As versões portuguesas do CAM e do FAM-CAM foram desenvolvidas com base em pressupostos metodológicos necessários para assegurar a sua validade e fiabilidade, revelando boas propriedades psicométricas e, nesta medida, considerou-se terem sido alcançados os principais objectivos da investigação.

O presente estudo, procurou contribuir ainda com uma actualização teórica e sistematizada dos principais aspectos clínicos do delirium no idoso, bem como uma revisão dos instrumentos de avaliação disponíveis.

Um outro aspecto relevante neste estudo prendeu-se ainda, com a caracterização minuciosa desta amostra do ponto de vista das diferentes variáveis sócio-demográficas, familiares e clínicas e, sobretudo, da relação destas com o desenvolvimento do delirium.

O estudo é inovador em Portugal pela validação do CAM e FAM-CAM, de uma forma estandardizada, obedecendo às linhas orientadores internacionalmente definidas para investigações deste âmbito.

A presente versão Portuguesa do CAM revelou-se como um instrumento válido na detecção do delirium em idosos hospitalizados. Além disso, sendo um dos mais amplamente usados em todo o mundo, a sua inclusão na prática clínica e em projectos de investigação permitirá uma uniformização de procedimentos, possibilitando a comparação com resultados obtidos em estudos internacionais.

Este instrumento deverá contudo, estar integrado num protocolo sistemático, abrangente e estruturado, com estratégias de prevenção e de actuação bem definidas, para assegurar uma maior eficiência em termos clínicos e económicos, bem como a sua implementação adequada em contexto de estratégias educativas, ao nível dos profissionais de saúde e familiares e/ou cuidadores.

A adopção destes protocolos pelas instituições de cuidados de saúde em Portugal não é ainda uma rotina ou pelo menos prática corrente. Por isso, torna-se crucial para a detecção precoce e tratamento do delirium, a definição de normas de orientação (com especial ênfase nas populações e contextos de elevado risco), a criação de protocolos formais a integrar em estratégias futuras de desenvolvimento de um Plano Nacional para as Demências.

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